Endocrinology

Version 5.3

Corrected, Updated, Lighter

PLAB 1 Keys is for PLAB-1 and UKMLA-AKT (Based on the New MLA Content-Map)

With the Most Recent Recalls and the UK Guidelines

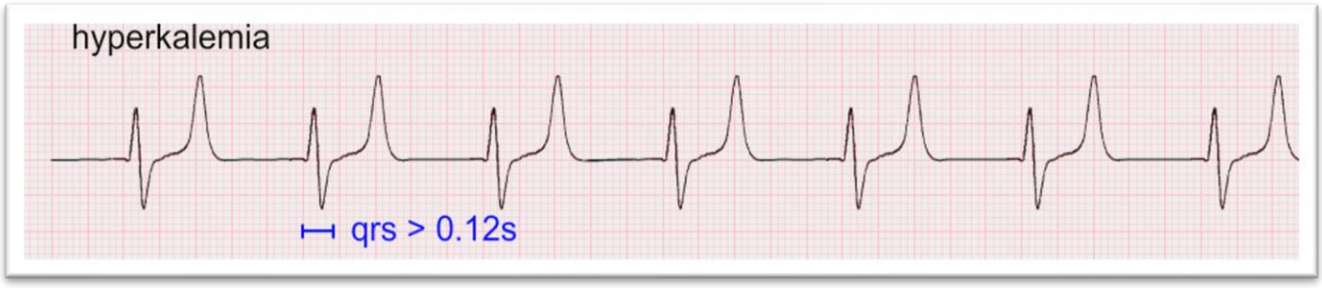
ATTENTION: This file will be updated online on our website frequently!

(example: Version 2.5 is more recent than Version 2.4, and so on)

Key 1	**Thyrotoxicosis (Hyperthyroidism) in pregnancy:** * *Propylthiouracil* is preferred preconception (*before pregnancy if a woman is planning to get pregnant*) and in the first trimester and postpartum. * *Carbimazole* is preferred in 2nd and 3rd trimesters + in general (non-pregnant). * Carbimazole: risk of aplasia cutis and omphalocele in the fetus. * Propylthiouracil: risk for hepatotoxicity in the mother. * Both drugs can cross the placenta; so, use the lowest possible dose.

	* Radioiodine therapy is contraindicated during pregnancy. * If hyperthyroidism cannot be controlled by drugs → Partial thyroidectomy can be done in the 2nd trimester. However, the safest Rx modality for pregnant women with hyperthyroidism is by giving antithyroid medications (e.g., PTU).
Key 2	2ry adrenal insufficiency (mostly iatrogenic). • After a long period of steroids intake, a sudden cessation of steroid intake will lead to 2ry adrenal insufficiency (iatrogenic). • Look for unexplained abdominal pain + nausea, vomiting ± *postural hypotension* ''Dizziness, Falls''. Note that (1ry adrenal insufficiency = Addison's disease, will be discussed in the coming keys).
Key 3	Diabetic ketoacidosis: - Occurs mostly in DM type 1 **- Presentation**:

	Abdominal pain, *vomiting*, *Kussmaul breathing* (deep hyperventilation), *dehydration*, *glucose>11*. **- Management**: √ Initially → IV fluids √ followed by IV infusion of insulin + measure arterial blood gases (ABG). "Sometimes, ABG is not given, instead, VBG is given -venous blood gases-" N.B. Sometimes, these options are not given, pick (measure capillary blood glucose) Obviously! - Dx: (pH < 7.3), ketonemia > 3 or ketonuria ++, Glucose > 11, Bicarb < 15 The initial fluid therapy in a patient with diabetic ketoacidosis is: → 500 ml of 0.9% sodium chloride over 15 minutes. "bolus". (0.5 L, not 1 L).
Key 4	• Normal Ca + Normal Phosphate + Normal ALP ➔ **Osteoporosis**. • Normal Ca + Normal Phosphate + High ALP ➔ **Paget's disease**. • Low Ca + Low Phosphate + High ALP ➔ **Osteomalacia**.

	Ca = Calcium, ALP = Alkaline Phosphatase
Key 5	**Hyperkalemia with ECG changes:** - Tall Tented T wave, Prolonged QRS → - Firstly, protect the cardiac membrane by giving *IV Calcium Gluconate* (OR: *Calcium Chloride*). - Then, reduce the serum Potassium by giving insulin with dextrose OR sometimes salbutamol inhalation.  Tall Tented T wave, Prolonged QRS → Hyperkalemia Once these ECG changes occur → give IV calcium gluconate or calcium chloride
Key 6	**Acromegaly:** ◙ In acromegaly, there is excess growth hormone (GH) secondary to a pituitary adenoma in over 95% of cases.

◙ **Some important features**:

- Bitemporal hemianopia, "due to compression on optic chiasm".
- spade like hands,
- enlarged nose and jaw.
- large tongue,
- prognathism "an extension or bulging out (protrusion) of the lower jaw (mandible)"
- interdental spaces
- Headaches, Hypertension, Sweating.

◙ Initial (screening) test and F/U test

→ IGF-1 (insulin like growth factors).

◙ The most definitive (confirmatory test)

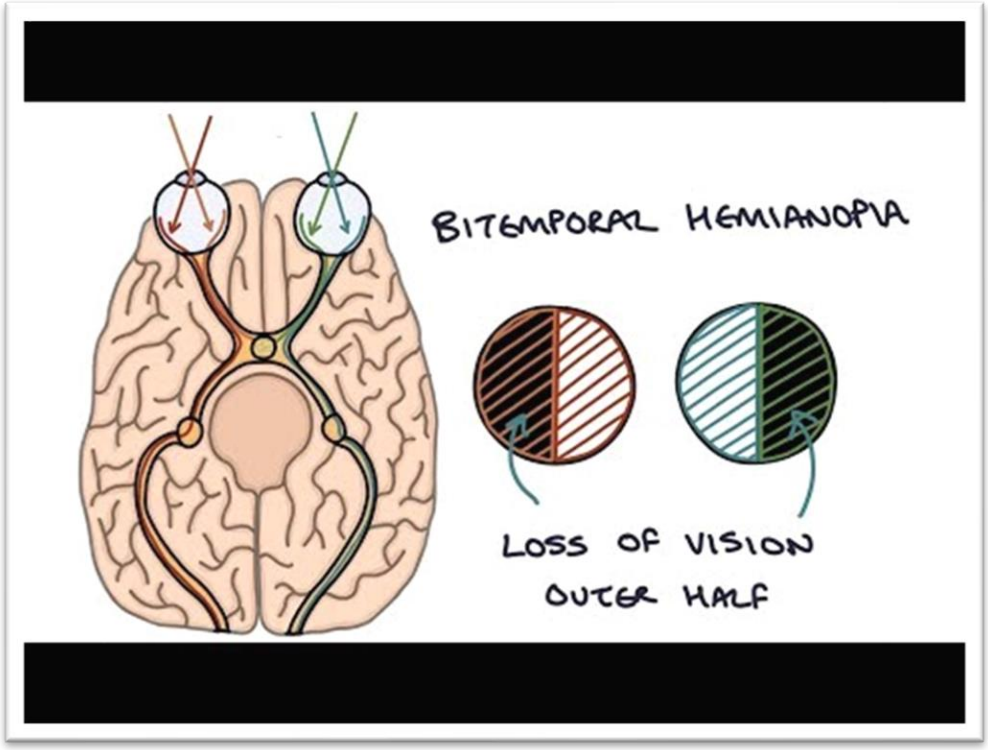
→ OGTT with serial Growth Hormone measurements.

OGTT = Oral Glucose Tolerance Test

N.B

In normal people, Growth hormone is suppressed by Glucose.

In acromegaly, Growth hormone is not suppressed by Glucose.



Note, bitemporal hemianopia (due to compression of the pituitary tumor on the optic chiasma) is seen in several conditions, importantly:

√ Acromegaly.

√ Hyperprolactinemia (e.g., pituitary macroadenoma).

Headaches + Hypertension + Sweating

+ ↑ Insulin-like growth factor (IGF-1)

Think → Acromegaly.

Key 7

Hypercalcemia with Prostate cancer.

- **Hypercalcemia manifestations:**

  Polyuria, polydipsia (↑ thirst), confusion, depression "low mood", kidney stones, abdominal pain, constipation, bone pain

  (Moans, Groans, Stones, Bones).

- **In a prostate cancer patient with these manifestations, initially order → serum calcium.**

- **The main causes of hypercalcemia:**

  1ry hyperparathyroidism, Malignancy, Sarcoidosis, TB

- **Initial management of hypercalcemia**

  → Rehydration with IV fluid 0.9% normal saline (0.9% NaCl).

- Then: Bisphosphonates (e.g. Alendronate, Risedronate, Pamidronate).

Key 8	**Amenorrhea with HYPOTHYROIDISM:** - Hypothyroidism Features: Weight gain in spite of decreased appetite, intolerance to cold, lethargy, puffy face, hands and feet (myxoedema), bradycardia, dry coarse cold skin, constipation, hair loss. N.B. initially, there is menorrhagia (↑ menstrual bleeding) followed by oligomenorrhea or amenorrhea. The note to remember from this key is that Amenorrhea can be associated with Hypothyroidism. • The Commonest cause of Hypothyroidism in the UK → *Autoimmune hypothyroidism* (Hashimoto thyroiditis). Sometimes, Hashimoto thyroiditis is given in the options instead of hypothyroidism. Pick it if the features are suggestive. • The Commonest cause worldwide: *iodine deficiency* (nutritional cause) (In both causes, there is usually goitre)

Key 9	Hyperprolactinemia (Milk discharge in non-pregnant woman + Amenorrhea) The main cause → Pituitary Adenoma → do MRI brain. MRI may also show Pituitary Adenoma pressing the optic chiasma, leading to a visual defect, which is → Bitemporal Hemianopia. - Remember: in pituitary adenoma and acromegaly, the visual defect is → *Bitemporal hemianopia*. - Remember: Hyperprolactinemia → Amenorrhea (low FSH and LH), Galactorrhea (Milk-discharge from nipple).
Key 10	Diabetic patient suddenly collapsed and fell unconscious → Request Random Blood Glucose. If blood sugar is below 4 mmol/L → It is hypoglycemia

Hypoglycaemia, clinically significant when blood glucose levels fall below 4 mmol/L, can impair cognitive function, particularly when levels drop below 3.0 mmol/L. In any patient presenting with altered consciousness, confusion, or coma, hypoglycaemia should always be considered.

Important Features of Hypoglycemia

→ (*Tachycardia, Sweating, Confusion, Trembling, Altered Mentation*).

♦ Management of Hypoglycemia (Important) ♦

Can swallow = can tolerate orally, not vomiting.

- If Conscious and Can swallow (can tolerate orally)

→ give 200 ml fruit juice Or Oral glucose gel.

- If Unconscious OR Conscious but Cannot swallow

→ IV Glucose (In case of IV access is already put).

OR IM or SC glucagon 1 mg (2 tubes) (In case of IV line is not available or not put yet or difficult to put as in patients who are having seizure/ convulsions).

Bear in mind that unconscious is different from confused.

◙ In-Hospital Management of Hypoglycemia (Summary):

• If the patient is confused but able to swallow → glucose gel (can be squeezed into the mouth between the teeth and gums).

• If the patient is confused and unable to swallow → IM glucagon or if there is already an IV line then give IV glucose.

Sometimes, a question will not tell you if the patient is able to swallow or not. However, you may find in the stem that the patient has been vomiting. Thus, he cannot swallow (cannot tolerate orally).

Examples of Used Concentrations (Important):

IV Glucose		
Over 10 minutes	75 ml of 20% glucose	150 ml of 10% glucose
Over 15 minutes	100 ml of 20% glucose	200 ml of 10% glucose
Every 1-2 minutes	50 ml of 10% solution given every 1-2 minutes until patient is conscious or 250 ml has been given (5 times repetitions).	

Important notes

√ Glucagon is ineffective with alcohol-related hypoglycemia. So, if the cause of hypoglycemia is alcohol → insert IV access and administer IV glucose.

√ Oral glucose gel should never be used in unconscious patients because of the fear of chocking.

	◙ Some Causes of Hypoglycemia: • Alcohol • Liver failure (impaired gluconeogenesis). • Excess paracetamol or aspirin. • Sulphonylureas (e.g., glibenclamide, gliclazide).
Key 11	Glycosuria (glucose in urine) is *NORMAL after Surgery* due to *stress* which increases the cortisol secretion and thus leads to hyperglycemia. - This is called → Stress Hyperglycemia. - *It resolves on its own in a few days post-op.*
Key 12	SCC (squamous cell carcinoma) of the lung leads to → *Hypercalcemia*. - This occurs (due to paraneoplastic effect as SCC releases parathyroid like molecules (PTH) like molecules → hypercalcemia. Important: • Small cell lung cancer → High ADH (AntiDiuretic Hormone) → *SIADH* → ''dilutional'' Hyponatremia and Hypokalemia.

	• It can also cause High ACTH → (*Cushing*). Important: • SCC of bronchus (lung) → PTH like molecules → Hypercalcemia. In sort: • Small cell cancer of the lung → SIADH & Cushing. • SCC of the lung → Hypercalcemia.
Key 13	DM type 2 in an obese patient with impaired renal function. → Give *insulin* (or) *Gliptins* (*DDP4 inhibitors*) Why the other options are contraindicated in this patient? • Biguanides (metformin): although it reduces weight and it is considered the first line hypoglycemic drug for DM type 2, it is contraindicated in renal impairment (GFR< 30) and the dose should be reduced if GFR<45. • Sulphonylureas (e.g., Gliclazide): is also contraindicated in renal impairment as it increases the risk of hypoglycemia

	+ it increases weight and the patient is already obese. √ With bad kidneys, avoid MS (Metformin, Sulfonylurea) • Glitazones (Pioglitazone): it increases weight. • SGLT-2 inhibitors: Contraindicated if GFR<60
Key 14	2ry amenorrhea (cessation of menstruation for > 6 months after it has been established) that occurs with *stress*, *excessive exercise* or *significantly low BMI* If 2ry amenorrhea develops after one of these conditions (stress, excessive exercise, low BMI)→ Think of hypothalamic Amenorrhea - Hypothalamic failure can occur in (stress, excessive exercise, low BMI). - In Hypothalamic Amenorrhea → HIGH PROLACTIN. - In hypothalamic failure → ↓ GnRH (Gonadotropin releasing hormone) → ↓ FSH, ↓ LH (with often subsequent ↓ estrogen). - To sum up:

	If a lady presents with amenorrhea (after it has been established) + Hx of stress/ excessive exercise (e.g., a runner, a sports lady) Think → Hypothalamic Amenorrhea. "imp"
Key 15	**Pheochromocytoma**: - A rare adrenal tumour secreting catecholamines (epinephrine and norepinephrine). - The key word is (EPISODIC). - Features: HTN (Hypertension), headache, sweating, tremors, palpitations, anxiety. **Mnemonic** PHEochromocytoma: • P → Palpitations • H → Headache, Hypertension • Ph → Flushing (sweating) • E → Episodic (Paroxysmal). **Q) What is raised in Pheochromocytoma?**

	Catecholamines, ie, epinephrine (adrenaline) and norepinephrine (noradrenaline). * **Dx** → 24 hours collection of urine metanephrines (not catecholamines). If 24-hour metanephrines are not in the options, pick 24 hours catecholamine. * **To confirm** → MRI (look for adrenal tumour). * **Rx of choice** → Surgical resection of the adrenal tumour. * N.B. 7-10 days before the surgery, stabilize the Hypertension by giving *Alpha-blockers* (Phenoxybenzamine) followed by Beta-blockers (Propranolol) to prevent intra-operative hypertensive crisis.
Key 16	A case of: DM type 2 + Microalbuminuria + mild HTN + Hypercholesterolemia What to give? 3 medications to be given, which are:

	• *Metformin* (to control Blood glucose) + • *ACEi* (to reduce the BP and to slow the progression of the kidney damage ''evidenced by the microalbuminuria and DM type 2'' + • *Statin* (for hypercholesterolemia). Important: DM type 2 + HTN → always consider ACEi unless severe renal impairment exists. ACE inhibitors are reno-protective, and with DM, there is a risk for nephropathy. Thus, we give ACE inhibitors to slow the progression of nephropathy.
Key 17	A 54 YO man known case of DM and HTN on metformin, ramipril and bisoprolol. His blood pressure is 135/88 and his BMI is 30 kg/m2. His labs: Urea 7 (Normal: 2-7) ▌Creatinine 140 (Normal: 70-150) eGFR 65 (Normal >90) ▌HbA1c 52 (Target: < 48) **Remember these Important points:** ♦ If the patient has new Dx of DM 2, advice firstly for lifestyle modifications. If after this, his HbA1c is still > 48 → start 1 hypoglycemic (e.g., metformin). ♦ If the patient is already on Metformin, and his HbA1c is still high but < 58 Also → Advice for lifestyle modifications.

♦ If the patient is already on Metformin, and his HbA1c is ≥ 58
→ Add another hypoglycemic agent.

The patient in this stem belongs to the second point. He is already on metformin but still a bit hyperglycemic.

As his HbA1c is <58, the answer would be
→ continue the same management + encourage lifestyle and diet changes.
(Recently asked Q)

◙ So, when to advise for lifestyle modifications?

√ Newly diagnosed patient with DM 2. +

√ Already on metformin and his HbA1c < 58 (not very high).

◙ When to consider adding another hypoglycemic agent?

√ If he is on a hypoglycemic agent e.g. metformin but his HbA1c is ≥ 58.

A case of:

Uncontrolled DM 2 despite lifestyle changes + eGFR <30

+ Hx of Heart Failure + BMI ≥ 30 (obese)

◙ What to give?

→ Insulin

◙ Why the other options are not correct?

√ Biguanides (metformin) → contraindicated if eGFR < 30.

√ Sulphonylureas → contraindicated in obese + in impaired eGFR

√ Gliptins (DDP 4 inhibitors) → contraindicated in Heart Failure.

√ Pioglitazone (Glitazones) → contraindicated in obese, HF, Bladder cancer.

Important Mnemonics for Hypoglycemic Agents

- With bad kidneys (*GFR < 30*), do not use MS (Metformin, Sulphonylureas e.g. gliclazide, glibenclamide).
- The heart has 4 chambers, so with Heart Failure (and pancreatitis), do not use DDP4 inhibitors (gliptins).
- The Pie (Pioglitazone) comes with the die (Risk of bladder cancer). So, Pioglitazone has a risk for Bladder Cancer. Pioglitazone is also contraindicated in Heart Failure.
- Hypoglycemics that cause weight gain (↑) are SPR:

  (Sulphonylureas, Pioglitazone, Repaglinide).

  The rest cause weight loss (↓) except DDP4 inhibitor Which has no effect on the weight.

	• SPR without the P have risk of hypoglycemia: Sulphonylureas and Repaglinide.
Key 18	1ry Adrenal insufficiency (Addison's disease): • Low *Cortisol* and *Aldosterone*. • Features: A patient with: ✓ *Postural hypotension (dizziness and vertigo),* ✓ *Weakness and fatigue,* ✓ *Nausea, vomiting, abd pain,* ✓ *Hyperpigmentation of the skin* and *the mucous membranes*. • The commonest cause in the developed world → *Autoimmune*. • The commonest cause in the developing world → *TB (infection)*. Mnemonic: Hypotension, Hyponatremia, Hypoglycemia. The only hyper is K^+ (Hyperkalemia) and Hyperpigmentation. ± There is: Metabolic Acidosis.

◙ In Addison's disease (1ry adrenal insufficiency):

- *High ACTH* → Hyperpigmentation
- *Low Aldosterone* → Hyponatremia and Hyperkalemia
- *Low Cortisol*→ postural hypotension and Hypoglycemia.

Please, note that in secondary adrenal insufficiency (occurs mainly after sudden cessation of prolonged steroid intake), there is NO hyperpigmentation of skin and mucous membrane.

◙ Investigations of Addison's disease

♦ In a patient with suspected Addison's disease, the definite investigation is an → Short ACTH stimulation test (short Synacthen test).

Plasma cortisol is measured before and 30 minutes after giving Synacthen 250ug IM. Adrenal autoantibodies such as anti-21-hydroxylase may also be demonstrated.

♦ If an ACTH stimulation test is not readily available (e.g. in primary care), then sending a 9 am serum cortisol can be useful:

> 500 nmol/l makes Addison's very unlikely.

< 100 nmol/l is definitely abnormal.

100-500 nmol/l should prompt an ACTH stimulation test to be performed

♦ Associated electrolyte abnormalities are seen in around one-third of undiagnosed patients:

hyperkalaemia

hyponatraemia

hypoglycaemia

metabolic acidosis

◙ Management of Addison's disease

♦ Patients who have Addison's disease are usually given both glucocorticoid and mineralocorticoid replacement therapy.

This usually means that patients take a combination of:

√ Hydrocortisone: usually given in 2 or 3 divided doses. Patients typically require 20-30 mg per day, with the majority given in the morning dose.

√ Fludrocortisone.

♦ Patient education is important:

√ Emphasise the importance of not missing glucocorticoid doses.

√ Consider MedicAlert bracelets and steroid cards.

- Management of intercurrent illness

In simple terms, the glucocorticoid dose should be doubled.

Addisonian crisis = Adrenal Crisis

• Addisonian crisis, or adrenal crisis, is a potentially life-threatening condition that results from an acute insufficiency of adrenal hormones (glucocorticoid or mineralocorticoid) and requires immediate treatment.

• It is important to differentiate an Addisonian crisis from Addison Disease which has a more gradual course.

• An illness or acute stress can precipitate adrenal crisis in the setting of Addison's disease.

• Addison's Disease is a condition in which the adrenal glands do not produce enough steroid hormones and occurs over several months.

What is Acute adrenal failure (Addisonian crisis)?

Sometimes the signs and symptoms of Addison's disease may appear suddenly. Acute adrenal failure (Addisonian crisis) can lead to life-threatening shock.

Signs and symptoms of Addisonian Crises:

√ Severe weakness "excessive tiredness"

√ Confusion.

√ Pain in lower back or legs.

√ Severe abdominal pain, vomiting and diarrhea, leading to dehydration.

√ Reduced consciousness or delirium.

√ Hypotension.

√ High potassium (hyperkalemia) and low sodium (hyponatremia).

√ Hypoglycemia can also be seen.

i.e. shortage (↓) of 3S → Salt (low Na^+ but high K^+), Sugar, Steroids.

♣ Causes

• Sepsis or surgery causing an acute exacerbation of chronic insufficiency (Addison's, Hypopituitarism).

• Adrenal haemorrhage e.g. Waterhouse-Friderichsen syndrome (fulminant meningococcaemia).

• Steroid withdrawal.

♣ Management of Addisonian crises:

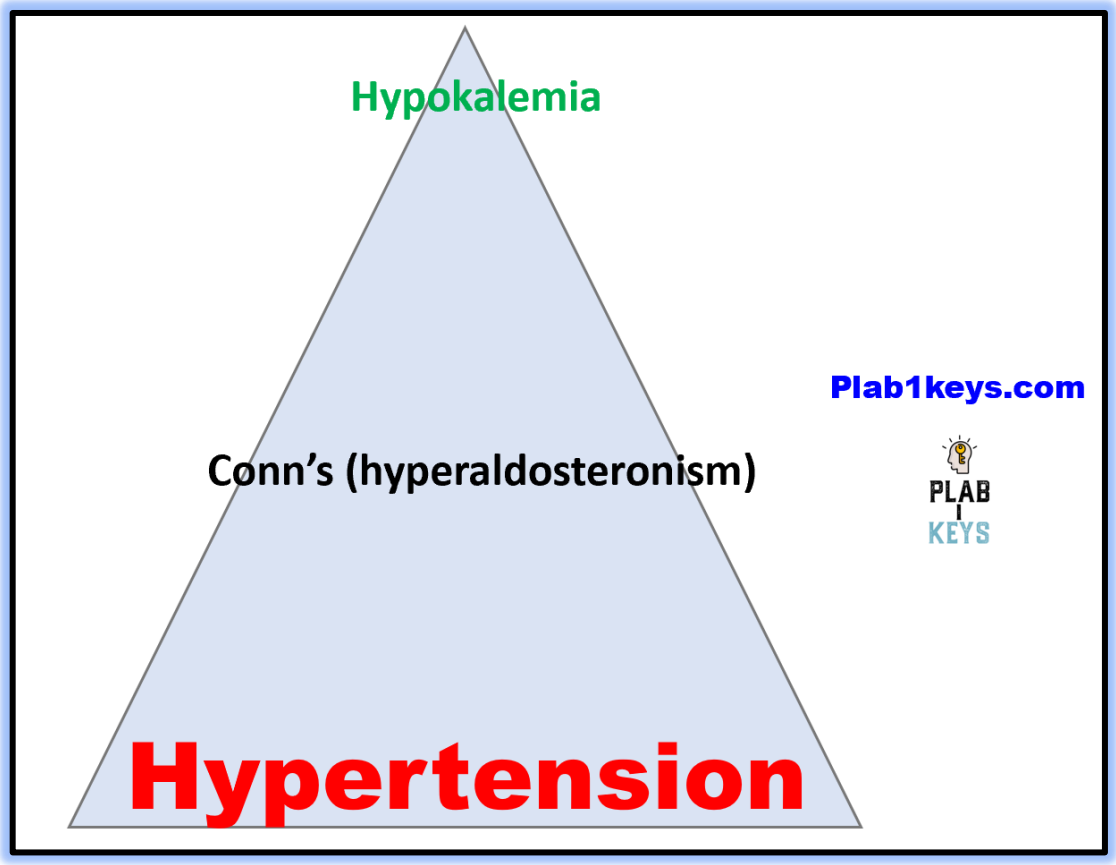
♦ First step → IV Hydrocortisone 100 mg (intravenously). Important √

	It can be given IM if no IV access is possible. Hydrocortisone would correct hypotension, hyponatremia and hyperkalemia. ♦ Then → 1 litre normal saline infused over 30-60 mins or with dextrose if hypoglycaemic. ♦ Continue hydrocortisone 6 hourly until the patient is stable. No fludrocortisone is required because high cortisol exerts weak mineralocorticoid action. ♦ Correct hypoglycemia if present. ♦ Oral replacement may begin after 24 hours and be reduced to maintenance over 3-4 days.
Key 19	Congenital Hypothyroidism • Important Complication → Jaundice √ Congenital hypothyroidism is rarely seen nowadays as there are screening tests when a baby is 6-8 weeks old (a part of the newborn blood spot test). √ If not corrected early, it may lead to some complications such as: • Prolonged Physiological Jaundice (starts after 24 hrs of birth and lasts for long time) • FFT (failure to thrive), • Short stature,

	• Impaired mental development • Broad Flat nose, widely set eyes, protruding tongue.
Key 20	DM type 1 with DKA presented unwell with altered level of consciousness and tachycardia with signs of dehydration (Dry MM, hypotension, slow capillary refill). First investigation → Capillary blood glucose THEN Arterial Blood Gas.
Key 21	Alcohol with HYPOGLYCEMIA. Alcohol is the commonest cause of hypoglycemia in adults followed by treated diabetes. - Scenario Example: A young adult was found outside a local pub with semiconscious level, profuse sweating, diaphoretic skin, GCS 12/15, tachycardia and hypotension. The likely diagnosis is → Hypoglycemia (He might have drunk so much alcohol → hypoglycemia). - Dx of Hypoglycemia: Whipple's Triad

	1) Low plasma glucose (usually < 4). **2)** Manifestations of hypoglycemia: e.g., sweating, confusion, tachycardia, hypotension, altered mentation. **3)** If blood glucose is corrected → rapid resolution of symptoms occurs.
Key 22	*Important Mnemonics for Hypoglycemics* • With bad kidneys (*GFR < 30*), do not use MS (Metformin, Sulphonylureas). • The heart has 4 chambers, so with HF (and pancreatitis), do not use DDP4 inhibitors (gliptins). • Also, the Pie (Pioglitazone) comes with the die (Risk of bladder cancer). So, Pioglitazone has a risk for Bladder Cancer. Pioglitazone is also contraindicated in HF. • Hypoglycemics that cause weight gain (↑) are SPR (Sulphonylureas, Pioglitazone, Repaglinide). The rest cause weight loss (↓) except DDP4 inhibitor Which has no effect on the weight. • SPR without the P have risk of hypoglycemia: Sulphonylureas and Repaglinide. • SGLT-2 inhibitors (Gliflozin) have increased risk for euglycemic DKA. • SGLT-2 inhibitors (Gliflozin) have an important side effect to remember → Genital infections eg, balanoposthitis (erythema and itchiness on the penis glans and prepuce).

Key 23	Hypokalemia + Hypertension → Think 1ry hyperaldosteronism = (Conn's syndrome). (Adrenal Adenoma)



Think of Conn's if:

- hypertension + Hypokalemia (e.g. muscle weakness) OR:
- Refractory hypertension despite 3 or more antihypertensive drugs OR:
- Hypertension before the age of 40 years.
- Other possible manifestations: Weakness, Lethargy, Headache.

◙ bilateral idiopathic adrenal hyperplasia is the cause in up to 70% of cases.

◙ Investigations of 1ry hyperaldosteronism (Conn's)

• Plasma aldosterone/renin ratio is the first-line investigation in suspected primary hyperaldosteronism.

• The aldosterone: renin ratio should be checked in primary hyperaldosteronism and should show high aldosterone levels alongside low renin levels (negative feedback due to sodium retention from aldosterone).

• Following this a high-resolution CT abdomen and adrenal vein sampling is used to differentiate between unilateral and bilateral sources of aldosterone excess

If asked about the most suitable hormone to order in a patient with Hypertension and Hypokalemia ± Headaches, weakness, lethargy

→ Aldosterone.

Another valid answer → Aldosterone : renin ratio.

◙ Rx: give aldosterone antagonist (e.g. Spironolactone) before considering surgery (Adrenalectomy).

	Conn's → excess (↑) Aldosterone → Hypertension, Hypokalemia (might be normokalemia), Normal Na+ or upper normal, Headache, Weakness ± METABOLIC ALKALOSIS ± Polyuria (due to aldosterone escape) **Remember**: √ In Addison's (↓ cortisol and aldosterone) → Hyperkalemia, Hypotension and Metabolic Acidosis. √ In Conn's (↑ Aldosterone) → Hypokalemia, Hypertension and Metabolic Alkalosis. √ In PHEochromocytoma (↑ catecholamines: adrenaline, noradrenaline) → The first three letters (PHE + F) Palpitations, Headache, Hypertension, Flushing (sweating), Episodic "attacks".
Key 24	**(◙) Pre-op Management of DM 2 (on oral hypoglycemics):** • If major surgery: Stop oral hypoglycemic the night before surgery. • If minor surgery: Continue the same routine.

	Alternative: if minor procedure (e.g., upper GI endoscopy) and the patient is on oral hypoglycemic e.g., gliclazide → Omit the morning dose, restart once the patient is eating and drinking again. **(◙) Pre-op Management of DM 1 (insulin-dependent):** • If major surgery: Start sliding scale IV insulin before surgery and continue until diet per-mouth is re-established. • If minor surgery: Omit insulin on the day of the surgery. *In all cases, restart the previous regimen when per mouth diet is re-established + Check Blood glucose 4 hourly.*
Key 25	**Diagnosing Diabetes** • **One** abnormal value, **+** DM **Symptoms** (polyuria, polydipsia, Unexplained wt loss in DM 1) **OR**: • **Two** Abnormal values **without symptoms**.

What are the abnormal values?

Fasting blood glucose (FBG) ≥ 7 mmol/L (≥ 126 mg/dL).

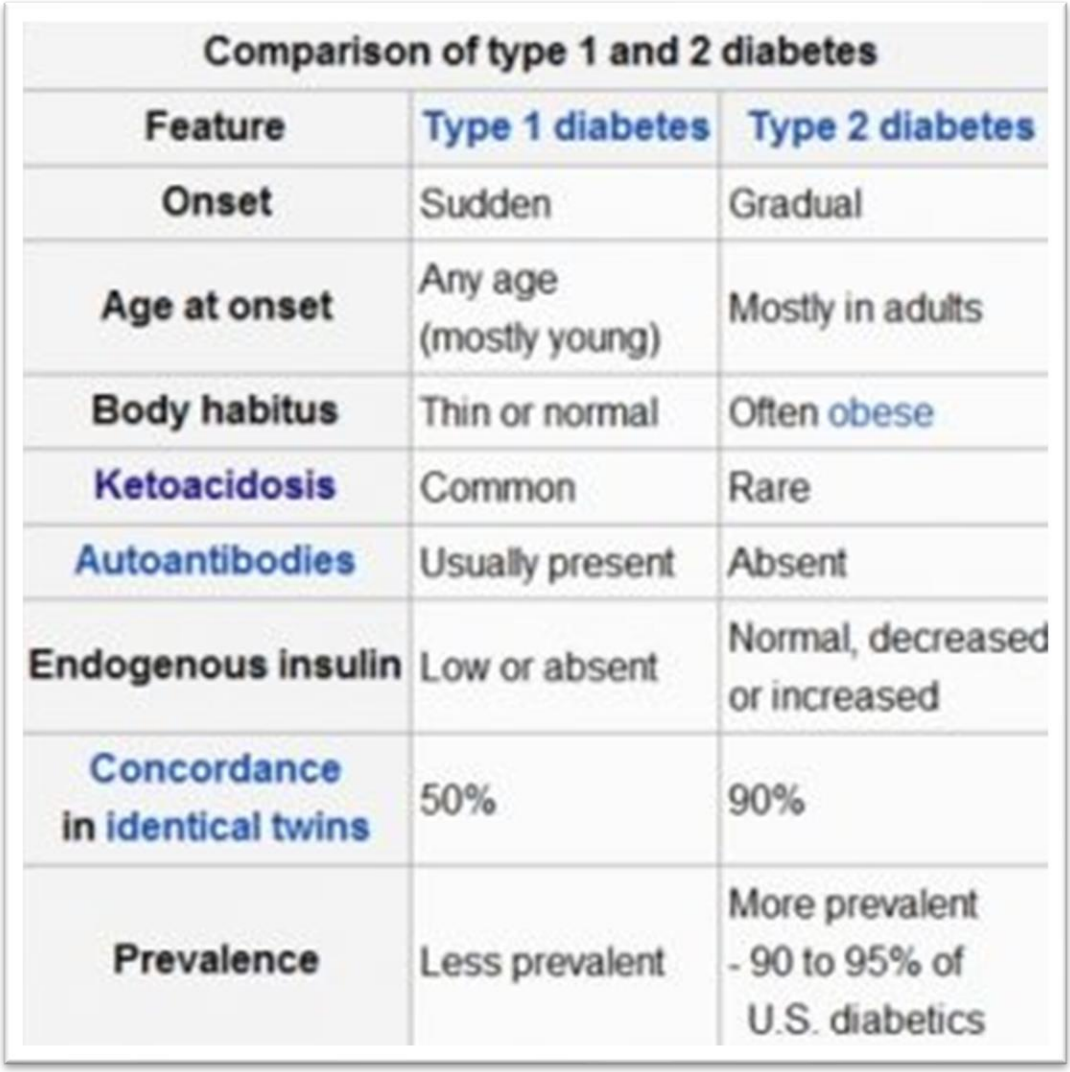
OR

Hb1Ac ≥ 48 mmol/mol (≥ 6.5%).

- Pre-diabetes (Impaired Glucose Tolerance):

Fasting → 5.5-6.9 ▌2-hour Post-Prandial → 7.8-11 ▌HbA1c → 42-47

- Note: **OGTT** (Oral Glucose Tolerance Test) is the diagnostic test for **gestational DM** (in pregnancy)

Comparison of type 1 and 2 diabetes

Feature	Type 1 diabetes	Type 2 diabetes
Onset	Sudden	Gradual
Age at onset	Any age (mostly young)	Mostly in adults
Body habitus	Thin or normal	Often obese
Ketoacidosis	Common	Rare
Autoantibodies	Usually present	Absent
Endogenous insulin	Low or absent	Normal, decreased or increased
Concordance in identical twins	50%	90%
Prevalence	Less prevalent	More prevalent - 90 to 95% of U.S. diabetics

Key 26	**(NOTE): Diagnosis of DM:** If a patient presents with polyuria, polydipsia, +ve glucose in urine → measure FASTING Blood Glucose, NOT RANDOM.

	Note, FBG is cheaper and is usually used while HbA1C is more expensive and so it is usually used if there is uncertainty. However, both are right options for diagnosing DM but the former is to an extent is more preferred.
Key 27	Alcohol can cause hypoglycemia (confusion, unable to speak, impaired GCS or even coma) Next Step → Check Blood glucose. √ **Remember, the causes of hypoglycemia (Glucose < 4):** * *Drugs*: sulphonylureas, excess paracetamol, aspirin. * *Alcohol intoxication*, *Liver failure* (impaired gluconeogenesis). * *Addison's disease* (hypoglycemia due to low cortisol).
Key 28	MODY (Maturity Onset Diabetes in the Young). • *DM < 25 Y/O* • *Strong FHx* (2 generations) • Mild Hyperglycemia • No need for insulin initially. Responds to Sulphonylureas. → Refer to endocrinology for

	→ Genetic counselling for maturity onset diabetes in the young (MODY). This is usually done before performing genetic tests.
Key 29	Addison's electrolytes: Low Na+, High K+ • Remember: in Addison's disease (1ry adrenal insufficiency), all are hypo except potassium: *Hyponatremia*, hypoglycemia, hypotension (Dizziness) + *HYPERKALEMIA* + N, V, Abd pain. Another hyper is tanned skin (Hyperpigmentation) but it is only seen in 1ry not 2ry adrenal insufficiency. • (Low Cortisol, Low Aldosterone). - High ACTH → Hyperpigmentation - Low cortisol → hypoglycemia and arterial hypotension - Low Aldosterone → Hyponatremia and Hyperkalemia - High K+ → High H+ → Metabolic Acidosis
Key 30	*Cushing's disease is <u>not</u> the same as Cushing's syndrome.* In Cushing disease (e.g., pituitary adenoma), excess ACTH is released from the pituitary gland and travels to BOTH adrenal glands making them secrete large amounts of cortisol. So, Bilateral (NOT UNILATERAL) adrenal hyperplasia might occur.

Remember, in Cushing's disease: ACTH is supressed by low (Overnight) or high dose of dexamethasone.

◙ Mnemonic for Cushing Syndrome Features:

"CUSHING"

• C – Central obesity, Cervical fat pads, Collagen fibre weakness "proximal muscle weakness", Comedones (acne), Cataract "due to hyperglycemia".

• U - ↑↑ Urinary free cortisol and glucose.

• S – Striae (Broad violaceous striae), Suppressed immunity (↑ infection liability).

• H – Hypercortisolism, Hypertension, Hyperglycemia, Hypercholesterolemia, Hirsutism

Hypertension usually that requires >2 antihypertensive agents.

• I – Iatrogenic (Increased administration of corticosteroids: a cause)

• N – Non-iatrogenic (Neoplasms: a cause)

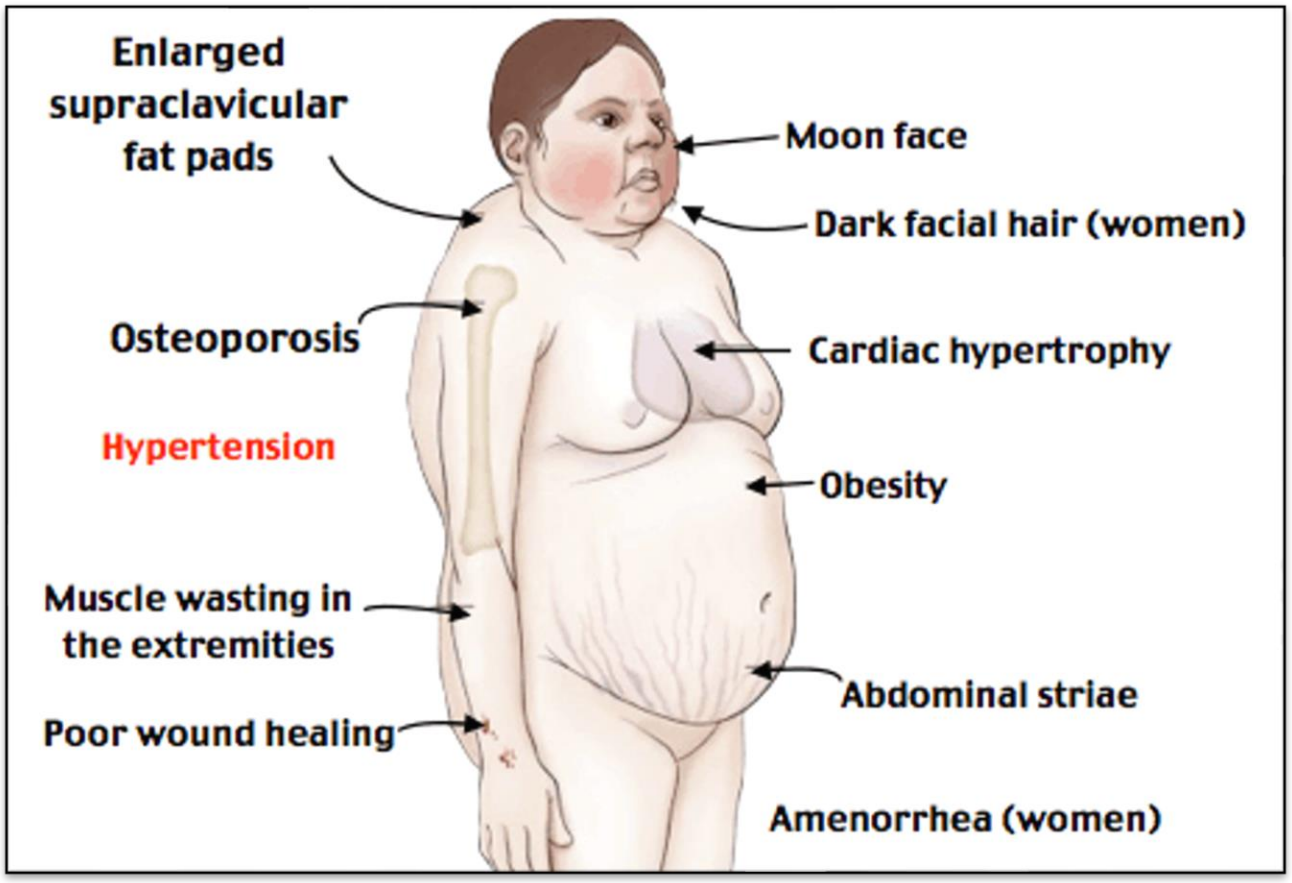
•G – Glucose intolerance, Growth retardation

Others: • Hypernatremia (↑Na^+) • Hypokalemia (↓K^+) • Easy bruising

• Moon face and buffalo hump "due to ↑fat"

• Cardiac hypertrophy • Osteoporosis • Weakness and fatigability

↑ cortisol → ↑ insulin resistance (cortisol is anti-insulin) → ↑ blood glucose



Cushing syndrome Investigations.

- The outpatient initial screening test → 24 hours urinary free cortisol.

- The best initial test to establish the Dx

  → 1 mg (low-dose) = Overnight Dexamethasone Suppression test.

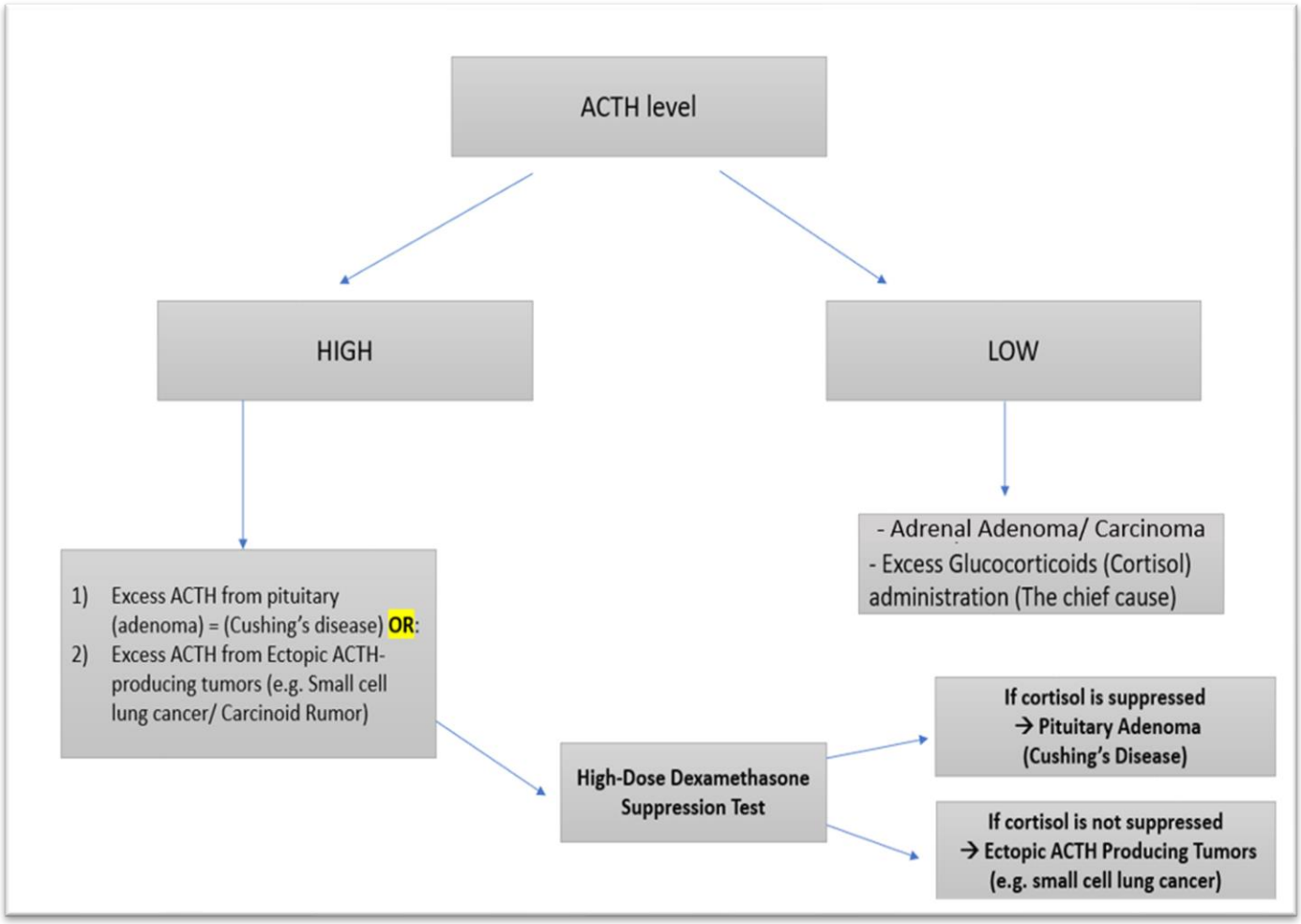
- To localise the lesion (to differentiate between pituitary adenoma and ectopic source → High dose dexamethasone suppression test.

◙ Explanation for Clarification

• Note that ACTH is released from pituitary gland while glucocorticoids (cortisol) is released from adrenal glands.

• Therefore, if ACTH is high, there is either pituitary adenoma (Cushing disease) or ectopic source that secretes ACTH such as small cell lung cancer. After performing high-dose dexamethasone suppression test, if the cortisol is suppressed, this means that the pituitary has stopped secreting ACTH (i.e. the problem is pituitary adenoma). Contrarily, if it is not suppressed, then there is another source of ACTH such as small cell lung cancer or carcinoid tumours.

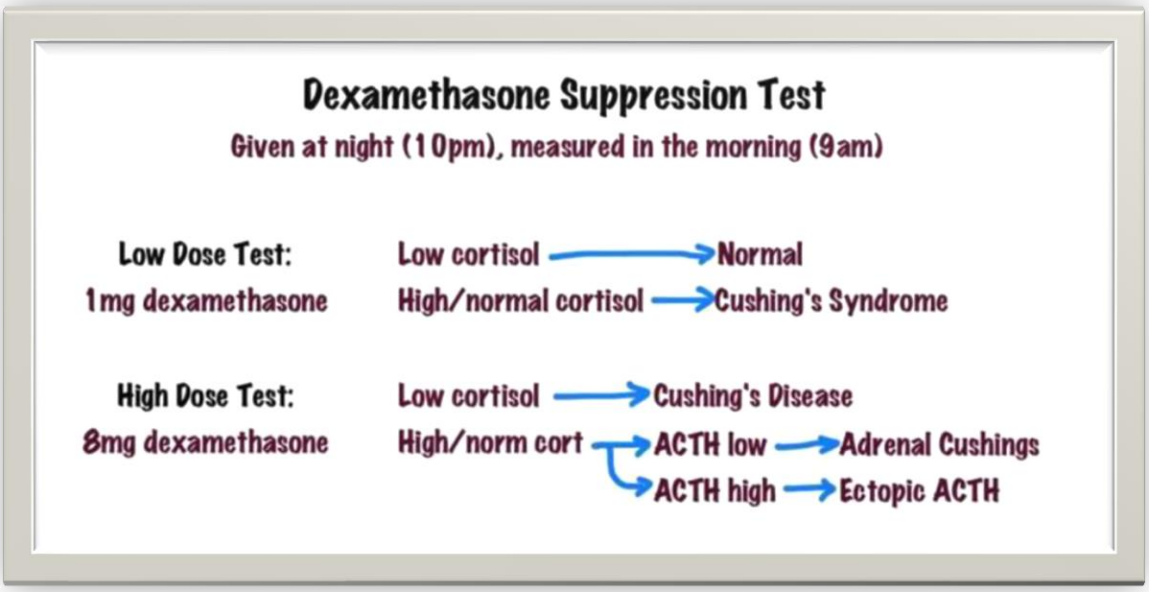
• On the other hand, if there is high cortisol, yet the ACTH level is low, then there is nothing to do with the pituitary gland. The problem is either adrenal adenoma (which secretes excess cortisol) or maybe the cortisol is being received from outside (excessive intake of cortisol).



√ ACTH is released from <u>pituitary</u> and from <u>ectopic ACTH releasing tumor</u> such as small cell lung cancer.

√ Cortisol (glucocorticoids) is released from <u>adrenal</u> glands.

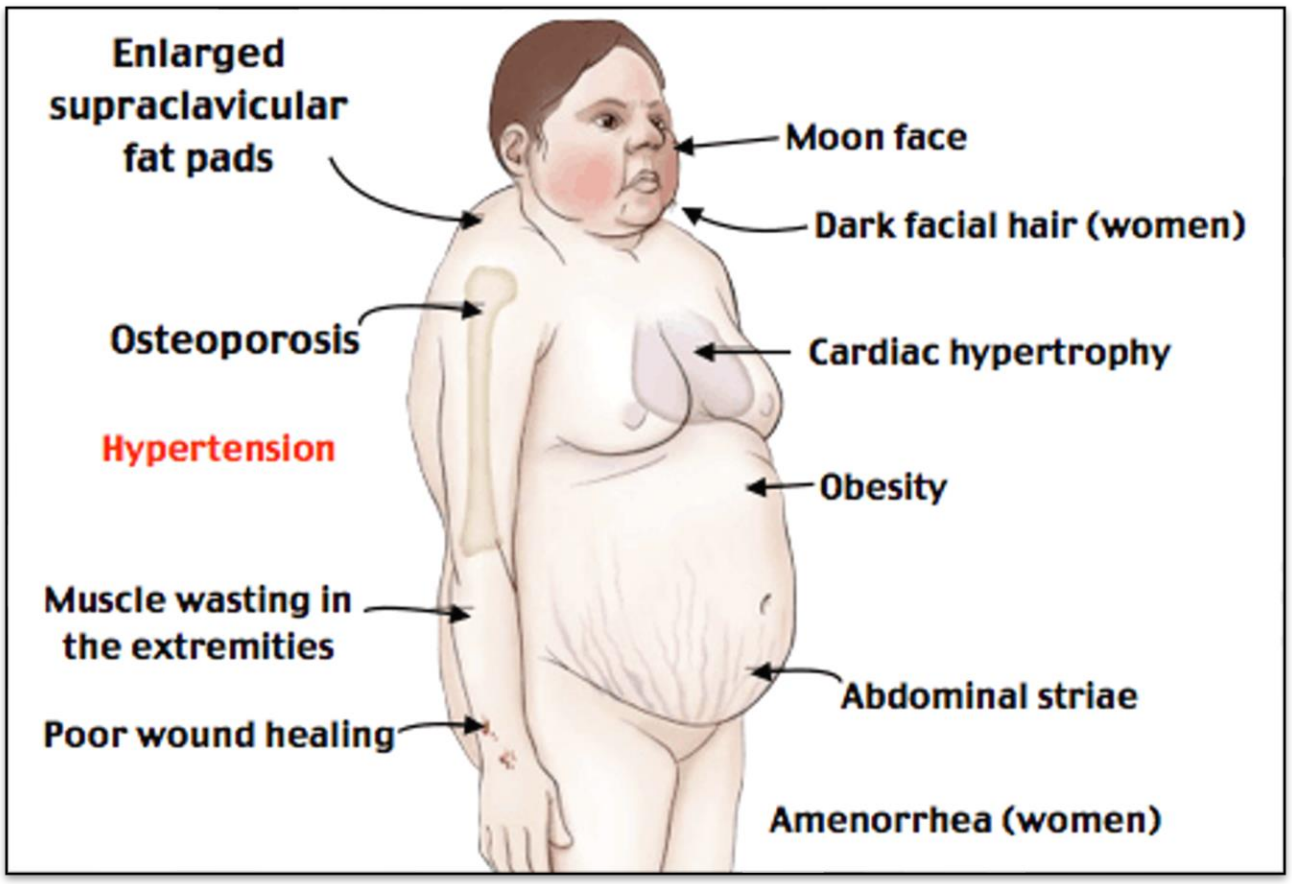
◙ If ACTH is low, this rules out pituitary and ectopic causes → the high cortisol is either due to adrenal tumor (go for adrenal CT), or excess cortisol intake.

	◙ If ACTH is high, go for high dose dexamethasone suppression test to know whether it is pituitary adenoma or ectopic tumor (e.g. small cell lung ca): √ If suppressed (low cortisol), this is Cushing disease → go for pituitary MRI. √ If not suppressed (still high cortisol), this is ectopic → CT chest, abdomen. 
Key 31	Vomiting → Metabolic Alkalosis (due to loss of H^+ -gastric hydrochloric acid-) → the body will keep CO2 which is acid to compensate the loss of H+ (by hypoventilation) → High pH (Alkalosis), High PCO2 (Compensatory Hypoventilation)
Key 32	Hyperkalemia can occur 2ry to Acute Kidney Injury (low eGFR) with ECG changes: Tall Tented T-wave and Widened QRS

	Initial step? → Protect the cardiac membrane before doing anything else by giving IV Calcium Gluconate or IV Calcium Chloride + Cardiac monitoring (as there are ECG changes).
Key 33	DM Diagnosis. The first thing to do in a patient with deep painless heel ulcer, polydipsia, polyuria, Wt loss, fatigue → request Blood sugar
Key 34	Stress Hyperglycemia: occurs in some diseases (e.g. Pneumonia, MI, Stroke) or post-op and resolves simultaneously soon.
Key 35	Severe post-op hyperkalemia (An important reason to remember is due to acute kidney injury 2ry to HF). Say that the K+ is >6.4 → we need to push it intracellularly quickly as this may lead to life-threatening arrhythmia → give insulin + glucose *Give 10 units insulin in 50 ml of 50% glucose IV infusion over 30 minutes* (N.B. *if calcium gluconate is in the options, give it first to protect the heart*)! √ Remember: crackles at lungs, sacral edema → think of Heart Failure (Do not give IV fluid)! He is already overloaded due to the HF!

	√ Remember: IV Insulin with Glucose will move K^+ inside the cells temporarily (for 2-6 hours). Therefore, IV NS (Normal Saline) needs to be given (if not an overloaded patient e.g. HF!) √ If the patient is well hydrated (fluid overload like in HF), start or increase the dose of loop diuretics (Furosemide) OR give Calcium Resonium. N.B. In Acute Renal failure + Anuria + severe Hyperkalemia (Especially if ≥ 7.5) → Consider ***Hemodialysis***.
Key 36	Breast cancer → bone metastasis → hypercalcemia (Drowsiness and increased thirst) N.B. Fluoxetine like all other SSRI (used for depression) can cause → Hyponatremia, however, *excessive thirst presents with hypercalcemia* not with hyponatremia. (be careful)!
Key 37	Addison's disease: low Na^+ but high K^+. Low cortisol and low aldosterone.

	Remember, in Addison's (high ACTH, low cortisol, low aldosterone): HypOnatremia, HypOglycemia, HypOtension, HypeRkalemia + Metabolic acidosis, N, V, Abd pain. + Hyperpigmented skin.
Key 38	*Cushing's disease is not the same as Cushing's syndrome.* In Cushing disease (e.g., pituitary adenoma), excess ACTH is released from the pituitary gland and travels to BOTH adrenal glands making them secrete large amounts of cortisol. So, Bilateral (NOT UNILATERAL) adrenal hyperplasia might occur. Remember, in Cushing's disease: ACTH is supressed by low (Overnight) or high dose of dexamethasone. ◙ Cushing features: *Hypertension that requires >2 antihypertensive agents,* *Truncal obesity,* *Hyperglycemia,* *moon* face, *striae,* *cardiac hypertrophy,* *osteoporosis,* *liability to infections*...etc



Key 39

Toxic nodular goitre.

- A lump on the front of the neck that moves on swallowing + manifestations of hyperthyroidism

  Think → Toxic nodular goitre.

- Some S&S of hyperthyroidism:

Palpitations, *tachycardia*, *intolerance to heat*, *weight loss* (unintentional weight loss despite having good appetite), *restlessness*, *nervousness*, *sweating*.

	√ **Note**, if the TSH is normal → non-toxic goitre (usually no symptoms). √ If **local compressive symptoms** (eg, **voice changes**, **difficult swallowing**) → Subtotal thyroidectomy.
Key 40	Panic attacks + Palpitations + Hypertension + Tremors → Think of pheochromocytoma • PHEochromocytoma: Palpitations, Headaches, Hypertension, Flushing, EPISODIC + Tremors and Anxiety. • It is a rare catecholamines secreting tumours (adrenal). • 10% bilateral 10% malignant 10% extra-adrenal 10% familial 10% without HTN. • Ix: 24-hour urine collection of metanephrines. • Surgical removal of the adrenal tumor is required, but 1-week pre-op, stabilize the Hypertension by *alpha-blockers* (e.g. *phenoxybenzamine*) followed by *beta-blockers* (*propranolol*)
Key 41	Subacute thyroiditis (De Quervain's Thyroiditis): - Tender and painful thyroid that may radiate to the lower jaw - (Remember: itis = painful), - No enlargement,

- Thyroid auto-antibodies → Negative (it is inflammation, not autoimmune disease).

- Radioactive iodine uptake test → decreased (depressed) radionuclide uptake.

(Note, in Graves' disease, radioactive iodine uptake is increased whereas in subacute thyroiditis it is decreased)

- As there is Negative thyroid Antibodies → it is neither (Grave's) nor (hashimoto). These 2 conditions are autoimmune (ie, have auto-Abs).

Subacute thyroiditis usually follows URTI (Viral). However, in some stems, this info won't be given. Instead, the stem would mention that the thyroid is PAINFUL and radioactive iodine uptake test is DECREASED.

The picture of subacute thyroiditis:

Initially: Hyperthyroidism (High T3 and T4, and low TSH, perspiration-sweating-, palpitations, tremors) followed by hypothyroidism.

- Remember: in Graves (Hyper) and Hashimoto (Hypo) → +ve thyroid antibodies.

- **Rx**: self-limited

As it is painful and inflammatory, **NSAIDs** can be used.

	Also, Beta-Blockers (e.g., **Propranolol**) can be used to control arrhythmia and palpitations "imp". • Note: the patient **won't** benefit from Carbimazole or propylthiouracil as subacute thyroiditis is a transient condition.
Key 42	**Thyroid storm (Thyroid crisis)** • Precipitated by infection (e.g., chest pneumonia): • Sick patient with low GCS, palpitations, tremors, tachycardia, feeling warm → (thyrotoxicosis). • Coughing, High temperature → (chest infection). • Atrial Fibrillation may be seen on ECG may occur 2ry to thyrotoxicosis. ◙ What to give to manage palpitations? → Beta-Blockers (e.g., Propranolol Oral or IV). ◙ The useful anti-thyroid medication in thyroid storm → Propylthiouracil. (*Remember that if there is no thyroid storm and no pregnancy, Carbimazole is the first-line medication for thyrotoxicosis*) ◙ N.B. Commence broad-spectrum IV Antibiotics as well for the infection.

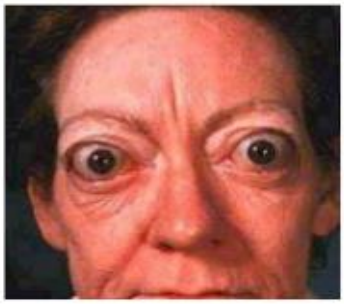
Key 43

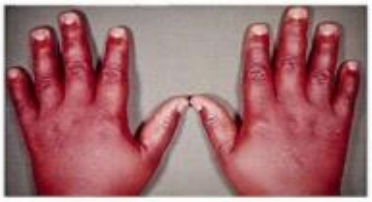
Eye signs of Grave's disease, what to do? → TFT

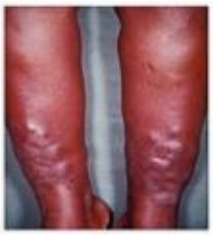
(Thyroid Function Tests are superior to Autoantibodies as we need to establish the diagnosis of hyperthyroidism before looking for its aetiology).

Graves disease

1. Eye signs – exomphalos, ophthalmoplegia, lid lag and lid retraction
2. Pretibial myxoedema
3. Thyroid acropachy







◙ Important Autoantibodies in Grave's Disease:

• Anti-thyroid stimulation hormone receptor antibodies (Anti-TSHR-Ab) are most specific for Grave's disease.

• Anti-thyroid peroxidase antibodies (Anti-TPO-Ab) can be found in Grave's but not specific for it. They are most commonly found in Hashimoto's thyroiditis (autoimmune hypothyroidism).

	◙ Important Notes on Diagnosing Grave's Disease: • The initial test for Grave's Disease is → Thyroid function test. • The most specific diagnostic test for Grave's disease is → Anti-thyrotropin receptor (Anti-TSH receptor) antibodies. On the other hand, anti-TPO antibodies are associated with various autoimmune diseases, not only Grave's.
Key 44	Hypoglycemic episode in a diabetic patient who presents with: Drowsiness, Confusion, Fatigue, Tremors, Blurred vision and Sweating. Immediately check (Random Blood Glucose). N.B. NOT Fasting blood glucose! NO TIME!
Key 45	(Tingling, numbness, paraesthesia, involuntary spasms of upper extremities) after Thyroidectomy → Hypoparathyroidism → Hypocalcemia √ When parathormone ↓ → serum calcium also ↓. √ (after surgical removal of thyroid, parathyroid gland/s may be removed or injured → ↓ Parathyroid hormone → ↓ Calcium). • **Hypocalcemia causes**: Osteomalacia (Vit D Deficiency), Chronic Renal Failure,

	Hypoparathyroidism (esp. post-op "Post Thyroidectomy"), Hypomagnesemia, Hyperphosphatemia. ↓ PTH → ↓ Calcium → ↑ Phosphate • **Features of Hypocalcemia:** SPASMODIC **Neuronal Hyperexcitability** Spasms, Perioral Paraesthesia, Anxious, Seizures, Muscle tones increased in smooth muscles, Orientation impaired and confusion, Dermatitis, Impetigo Herpetiform (rare and serious), Chvostek's sign, Cardiomyopathy (prolonged QT interval on ECG). - Trousseau's signs → after occlusion of brachial artery → *wrist flexion* - Chvostek's sign → Tapping over parotid → *twitching of facial muscles*. • Rx: give 10 ml of 10% Calcium Gluconate (initially).
Key 46	SIADH: Syndrome of Inappropriate Antidiuretic Hormone √ Can occur 2ry to *small cell lung cancer* → Water retention → Dilutional Hyponatremia → The patient is overloaded (overhydrated) √ Can also occur 2ry to *meningitis*.

	√ The mainstay Rx → Fluid Restriction. √ If failed → Tolvaptan or Demeclocycline.
Key 47	Subacute thyroiditis • Palpitations, tremors and sweating (features of hyperthyroidism) usually after URTI • Imp: it can also occur in a woman after birth (Postpartum Thyroiditis). **Postpartum thyroiditis:** An inflammatory condition of the thyroid gland, can occur after childbirth. It includes 2 phases: starts with hyperthyroidism (the treatment is supportive by giving **propranolol**: for palpitation, tremor, anxiety), and second phase is hypothyroidism (levothyroxine can be given if symptomatic hypothyroidism). Then, it returns to normal. • Thyroid is usually tender but not significantly enlarged. • T3 and T4 high or upper normal (hyperthyroid phase). • TSH low or lower normal, • Radionuclide uptake is depressed. ➔ Give Beta-blockers (propranolol) to control palpitations and tachycardia. N.B., *we give Beta-blockers in thyroid storm and subacute thyroiditis (for racing heart).*

Key 48	In all patients with severe hyperkalemia (K^+ more than 6.5), the INITIAL step is to protect the heart by giving IV calcium gluconate or IV calcium chloride. • *Do not get tricked by haemodialysis in the options. You need to protect the heart First!*
Key 49	Impaired glucose tolerance (PRE-DIABETES): • FBG: 5.5 – 6.9 (below 7) AND: • 2-hour Postprandial: 7.8 – 11
Key 50	A baby with severe dehydration (dry mucous membranes, sunken eyes and fontanelles, reduced skin turgor) + HypOnatremia + HypOkalemia. This could be due to: Sepsis or DKA or others. **What to give?** → IV fluids (0.9% Sodium chloride + Potassium chloride) N.B. Do not give Sodium chloride alone (this won't correct the low K+). N.B. Do not give Dextrose (as the patient might already have high glucose due to DKA).
Key 51	Hypothyroidism: Dry skin, lethargy, tiredness, weight gain, intolerance to cold, amenorrhea or oligomenorrhea…etc. • **Remember that:**

	In autoimmune hypothyroidism (Hashimoto's thyroiditis), the patient may have an associated autoimmune disease such as *Vitiligo*, *ADDISON'S* disease, *Pernicious Anemia*, *DM type 1.* Sometimes, Hashimoto thyroiditis is given in the options instead of hypothyroidism. Pick it if the features are suggestive. E.g., lethargy, fatigue, cold intolerance, dry skin, ↑TSH, ↓ free T4.
Key 52	Stress hyperglycemia: √ After surgery, stress, infections, trauma → high cortisol → high glucose → glycosuria (glucose in urine) √ This subsides on its own in a few days. ◙ What to do next as a follow up step? → FASTING blood glucose (although it is a normal phenomenon, we need to make sure of our diagnosis of the Stress hyperglycemia). ◙ What to do to know if it is DM or Stress hyperglycemia? → HbA1c "glycosylated haemoglobin" As it reflects the blood glucose over the previous 3 months.

Key 53	Stress hyperglycemia can occur after surgery or infection or trauma e.g. RTA. Do Fasting blood glucose when glycosuria subsides as a follow up investigation.
Key 54	A child who is obese, short, with abdominal striae with Hx of renal transplant. The likely cause of these features → Cushing Syndrome (High Cortisol levels) due to exogenous intake of steroids post renal transplant. The child is short because steroids are Anti-Vit D. Also, high cortisol leads to high blood glucose which inhibits GH (growth hormone). ↑ Cortisol → ↑ Glucose → ↓ Growth hormone
Key 55	The manifestations of thyrotoxicosis (tremors, anxiety, wt loss, tachycardia) are physio-pathologically due to → High Metabolic Rate
Key 56	Congenital hypothyroidism

	An infant with: prolonged neonatal jaundice (or FHx of prolonged neonatal jaundice), Constipation, dry skin, FTT (Failure to Thrive), Protruded tongue, flat nose, widely set eyes → Congenital Hypothyroidism. N.B. This is very rarely seen nowadays because screening for hypothyroidism is available early after birth by measuring TSH from the initial dried blood spot throughout the UK.
Key 57	**Prolactinoma** (↑↑ prolactin) due to pituitary adenoma √ Prolactinomas are a type of pituitary adenoma, a benign tumour of the pituitary gland. √ The major effect of prolactinoma is decreased levels of some sex hormones: *estrogen* in women and *testosterone* in men. ◙ Pituitary adenomas can be classified according to: √ Size (a microadenoma is <1cm and a macroadenoma is >1cm). √ Hormonal status (a secretory/functioning adenoma produces and excess of a particular hormone and a non-secretory/functioning adenoma does not produce a hormone to excess). Prolactinomas are the most common type and they produce an excess of prolactin.

◙ Features of excess prolactin:

- Men: impotence, loss of libido, galactorrhoea
- Women: amenorrhoea, infertility, galactorrhoea, osteoporosis

◙ Diagnosis:

- serum prolactin (Normally below 400), if ≥ 5000, then suspect Macroadenoma (prolactinoma).
- If > 2000, keep prolactinoma (even if Microadenoma) in mind.
- Others are low (FSH, LH, Oestradiol)
- Confirmatory test: MRI Brain. √

◙ **Prolactinoma Management:**

Pituitary macroadenoma + ↑ serum prolactin (± amenorrhea):

√ First line: Dopamine agonist (e.g., Cabergoline, Bromocriptine). They inhibit the release of prolactin from the pituitary gland.

Important: If you have to choose between these 2 dopamine agonists, pick →(**Cabergoline**) as it is 1st line and has higher efficacy and less side effects.

	If no response (ie, if these medications did not shrink the tumour and there is still hyperprolactinemia) → switch to the second line. √ Second line: Trans-sphenoidal surgery to surgically resect and remove the prolactinoma – the tumour- of the pituitary gland. (If medical therapy failed). • Note that: local manifestations caused by prolactinoma compressing the surrounding structures may include: → progressively worsening headaches, visual disturbance. • N.B. Cabergoline is more effective than Bromocriptine in normalizing prolactin in Microprolactinoma. • Other manifestations of hyperprolactinemia: → Galactorrhea, Amenorrhea or Oligomenorrhea, Headaches, Infertility, Visual disturbances; Bitemporal Hemianopias.
Key 58	Diabetic Neuropathy: A diabetic patient with poorly controlled hyperglycemia:

	- Loss of sensation (fine touch and pain) starts in toes bilaterally and ascends (gloves and stocking pattern). - Loss of Ankle jerk reflex bilaterally. Mechanism: Microvascular injury → Damage of nerves.
Key 59	DM type 2 medication if the patient is obese and eGFR < 30 and lifestyle modifications have been tried and FBG is still above 11.1: • Metformin? NO! metformin is contraindicated if GFR < 30 • Sulphonylureas? NO! it causes weight gain and the patient is already Obese. Plus, in renal impairment, sulphonylureas have a higher risk to cause hypoglycemia. • Low sugar diet? No! Lifestyle modifications have already been tried without benefits. • DDP-4 inhibitors (Gliptins)? YES! They Do not affect weigh and they are safe in patients with renal impairment. - N.B. Avoid DDP-4 inhibitors in HF and pancreatitis.
Key 60	Hypothyroidism commonest causes: • In the UK → Autoimmune (Hashimoto's thyroiditis). • Outside the UK -worldwide- → Iodine Deficiency. (Nutritional cause).

Key 61

DKA (Diabetic KetoAciosis)

Q) First immediate management?

→ IV fluids followed by IV infusion of regular Insulin

The initial fluid therapy in a patient with diabetic ketoacidosis is:

→ 500 ml of 0.9% sodium chloride over 15 minutes. "**bolus**".

Followed by a continuous rate "infusion":

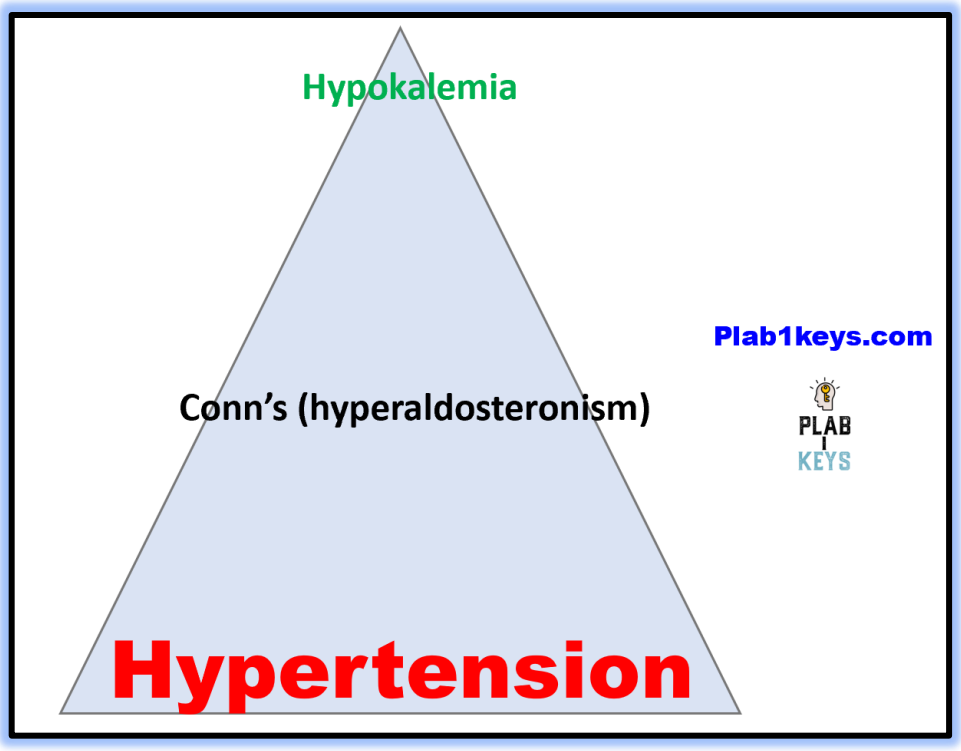
◙ Features:

Fruity smell breath (pearl drops), Abdominal pain, Nausea and Vomiting.

pH < 7.3 // Blood glucose > 12 or a known diabetic // Bicarb < 15 // Ketonemia > 3 or Ketone bodies in urine dipstick ++

N.B. When blood glucose reaches below 12, shift IVF NS to 5% dextrose to avoid hypoglycemia (due to rapid correction of the hyperglycemia).

N.B. Hypokalemia may need to be corrected with KCl (Potassium Chloride) after giving the first litre of IV normal saline.

Key 62	Hypokalemia + Hypertension → Think of Conn's syndrome (hyperaldosteronism). Therefore, the first hormone level to order is → Aldosterone. As for the treatment: Give Aldosterone antagonist (e.g. Spironolactone) before considering surgery (Adrenalectomy). 
Key 63	In prolactinoma (pituitary adenoma) → (Hyperprolactinemia) → Amenorrhea, Galactorrhea → Start drug therapy before surgery → Dopamine Agonists (e.g. Cabergoline, Bromocriptine).

	If no response → Transsphenoidal surgery to remove the pituitary adenoma.
Key 64	DM type 2 in an Obese (BMI > 30) patient without significant renal impairment (eGFR above 45) → Start with Biguanide (metformin = Glucophage). • N.B. (SPR) cause weight gain Sulphonylureas (e.g. Glibenclamide, Gliclazide), Pioglitazones (Glitazones) and Repaglinide → Weight gain. • As long as GFR is acceptable, the preferred option → Biguanide (metformin). **Other cases:** - Obesity only → Biguanide (Metformin) - Obesity + Significantly impaired kidneys → DDP-4 inhibitors (Gliptins), if no response → Insulin. - Impaired kidneys alone → DDP4-inhibitors (Gliptins e.g., Linagliptin, Sitagliptin) or Repaglinide or Pioglitazone.

Key 65	• Remember that: √ ACE inhibitors (e.g., Ramipril) and √ Potassium sparing diuretics (e.g., Spironolactone) can cause → hyperkalemia. • Mild hyperkalemia (5.5-5.9) • Moderate: (6-6.4) • Severe (> 6.5) - If mild hyperkalemia, no abnormalities on ECG, then the best initial step → *Stop the medications* causing hyperkalemia (e.g. ACEi, Spironolactone). - If moderate, severe, and/or ECG changes: Tall Tented T wave, we firstly need to protect the cardiac membrane from possible fatal arrhythmia → Calcium gluconate or calcium chloride IV. - After that, insulin with dextrose OR even nebulized Salbutamol can be given to shift the potassium intracellularly.
Key 66	PHEochromocytoma: *Excess catecholamines (adrenaline and noradrenaline) due to adrenal adenoma.* • P → Palpitations

	• H → Headache, Hypertension • Ph → Flushing (sweating) • E → Episodic (Paroxysmal).
Key 67	Osteomalacia • Alkaline phosphatase is high, • Ca^{++} and Phosphate are low. • Proximal muscle weakness. Sometimes, the stem may only give you that Alkaline phosphate is high without mentioning that the patient has low calcium or phosphate. In this case, other hints towards low Vit D will be given. For examples, muscle aches, proximal muscle weakness, the patient does not go out frequently (lack of exposure to sunlight), poor diet (not enough Vit D intake). N.B. Proximal muscle weakness and pain are features of Vit D deficiency; thus osteomalacia. In **osteomalacia**: the patient should be prescribed both: vitamin D and calcium supplements.

	However: If you have to pick one of the two, pick vitamin D supplements. (Important √). ** IMPORTANT NOTE: Whenever you see an ISOLATED High Alkaline Phosphatase, think of 2 Bs + P: 1) Bone: Osteomalacia, Paget's disease, Hyperparathyroidism, Bone metastases. 2) Biliary tract: Cholestasis (Obstructive Jaundice). 3) Pregnancy (Physiological finding). **Remember**: • Normal Ca + Normal Phosphate + Normal ALP → **Osteoporosis**. • Normal Ca + Normal Phosphate + High ALP → **Paget's disease**. • Low Ca + Low Phosphate + High ALP → **Osteomalacia**.
Key 68	Peri-oral paraesthesia + facial muscles twitching → Hypocalcemia. This can occur in diabetic patients. How? DM → Diabetic Nephropathy → Chronic Renal Failure → Hypocalcemia.

	The causes of Hypocalcemia: - Vit D deficiency (Osteomalacia) - Chronic Renal failure - Hypoparathyroidism (Post-thyroidectomy or parathyroidectomy) - Hypomagnesemia - Hyperphosphatemia. - Panic attacks → Hyperventilation → transient hypocalcemia. • Rx: give 10 ml of 10% Calcium Gluconate (initially) • N.B. The kidney is the main site for the conversion of 25-hydroxyvitamin D (25D) to circulating calcitriol.
Key 69	DI (Diabetes Insipidus) Could be Cranial (Central) or Nephrogenic. • Low urine osmolality. • After giving Vasopressin → there will be an increase in urine osmolality (as it is initially low in DI) → This is diagnostic for Central (Cranial) DI.

- If no changes after Vasopressin (still urinating large volumes with low urine osmolality and high serum osmolality) → Nephrogenic DI.
- After fluid restriction → If still urinating high volumes and urine osmolality is still low → it is DI → Give Vasopressin and see the result as above.

In SIADH:

Hyponatremia (low Serum Sodium), Low Serum Osmolality, High Urine Osmolality.

In Diabetes Insipidus:

Hypernatremia (high serum sodium), Low Urine Osmolality, High Serum Osmolality. *(The urine osmolality increases after giving vasopressin)*

What is the low?

In SIADH → Sodium and Serum osmolality.

In DI → urine osmolality.

You may remember this by knowing that Diabetes Insipidus is defined as "the passage of large volumes (>3 L/24 hr) of dilute urine (< 300 mOsm/kg)".

Dilute urine = Low Osmolality Urine.

In Psychogenic Polydipsia:

Low to normal Urine Osmolality, low to normal Serum Osmolality.

	Urine osmolality	Serum osmolality
SIADH	High	Low
Diabetes insipidus	Low	High
Psychogenic polydipsia	Low to normal	Low to normal

♦ DI → DIencephalon.
♦ SIADH → Cerebrum/ Cerebellum.

If still confused, read the following:

√ If you suspect diabetes insipidus, the initial test is

→ urine osmolality. (if < 800, then it is likely DI, we then proceed to plasma osmolality and fluid deprivation test). Imp √

√ To differentiate central from nephrogenic DI,

→ Fluid deprivation test is done followed by desmopressin/vasopressin administration. Imp √

What if you suspect DI but there is not (request urine osmolality) in the options? → pick fluid deprivation test and response to vasopressin.

◙ In normal people:

After fluid deprivation, the urine volume will decrease and the urine osmolality will increase (Normal: No fluid intake → Low urination, and the urine is concentrated i.e. high osmolality).

◙ In diabetes insipidus:

After fluid restriction, the urine volume will continue to be high and the urine osmolality will continue to be low.

Now, we administer IM vasopressin to determine the type:

◙ In Central "Cranial" DI:

After vasopressin administration → The urine volume will decrease and the urine osmolality will increase.

◙ In Nephrogenic DI:

After vasopressin administration → No change (The urine volume will remain increased and the urine osmolality will remain low).

IMPORTANT:

√ The INITIAL test in DI → Urine osmolality.

√ The test to differentiate between central and nephrogenic DI

→ Fluid deprivation test.

Example:

A head injury followed by increased urination (polyuria) and increased water drinking (polydipsia). Serum sodium is high (hypernatremia).

Think → Diabetes insipidus (cranial).

• Cranial diabetes insipidus can be idiopathic or due to head injury or pituitary gland surgery. The mechanism is that there becomes a decreased in the secretion of the antidiuretic hormone (ADH) from the pituitary gland).

	• In nephrogenic diabetes insipidus, there is normal secretion of ADH but there is insensitivity to ADH. • Note that in diabetes insipidus, there is hypernatremia (↑ serum Na+), whereas is SIADH and Addison's disease, there is hyponatremia.
Key 70	High prolactin (>2000), (Hypogonadism) + Amenorrhea + Infertility → Think of Prolactinoma. Remember: - In PCOS → LH: FSH ≥ 2 i.e. LH level is double the FSH level or more than the double. - In Premature Ovarian Failure (POF) (before the age of 40) → FSH is high *(>25 in two occasions 4 weeks apart*).
Key 71	SCC of the lung can cause → Hypercalcemia (due to the production of PTH like molecule). The INITIAL step to treat hypercalcemia is → IV 0.9% Normal Saline. √ imp.
Key 72	In Diabetes Insipidus (DI): - After Fluid Deprivation → Urine Osmolality Decreases, Serum Osmolality Increases.

	- After giving Desmopressin → Urine Osmolality Increases, but Urine Volume Decreases → (**Central** = Cranial DI). - After giving Desmopressin → No change → ((**Nephrogenic** DI)). - Diabetes Insipidus is defined as "The passage of large volumes (>3 L/24 hr) of dilute urine (< 300 mOsm/kg)". Dilute urine = Low Osmolality Urine.
Key 73	In *Asymptomatic* DM patient, 2 abnormal results are needed for diagnosis. e.g., if Fasting blood glucose is ≥ 7, we need to repeat FBG or to order HbA1C to confirm a diagnosis of DM. * Abnormal results include: FBG >= 7, or HbA1c ≥ 48
Key 74	In Addison's disease (Postural Hypotension, Hyperpigmentation, Abdominal pain and Vomiting) → Low sodium and high Potassium. Remember, the only hyper is hyperkalemia. Others are hypo: Hyponatremia, Hypoglycemia, Hypotension (low cortisol and low Aldosterone) = Adrenal insufficiency. Tip, Aldosterone is a friend of sodium. If aldosterone is low (such as in Addison's), there will be low sodium but high potassium.

Key 75	Hyperthyroidism (Tachycardia, Palpitation, Unintentional weight loss, Intolerance to heat …etc) may only present as a female with palpitations and wt loss. What to do? → order TFT (Thyroid Function Tests)
Key 76	Pheochromocytoma: Palpitations, headache, hypertension (sometime postural hypotension), Flushing (Sweating), episodic + Tremors *Postural hypotension* → a reduction in the Systolic BP of ≥ 20 mmHg within 3 minutes of standing. - If you see palpitations, sweating and then postural hypotension, pick pheochromocytoma as it sometimes occurs.
Key 77	Cushing's Syndrome features: *2ry Amenorrhea, Acne, hyperpigmentation, Obesity* (High BMI), *lethargy, Abdominal Striae, Hyperglycemia, Hypertension, Hypokalemia* …etc. • Remember that the last two mentioned features (*Hypertension* and *Hypokalemia*) are also present in Hyperaldosteronism ''Conn's''. However, Conn's has other features such as polyuria and polydipsia (due to aldosterone escape). Furthermore, Conn's does not present with Amenorrhea or Obesity. • N.B. Hypertension + Hypokalemia → Cushing or Conn's (Hyperaldosteronism). (2Cs).

Key 78	**Hyperprolactinemia in men:** Galactorrhea + Decreased libido + Erectile dysfunction **Hyperprolactinemia in women:** Galactorrhea, Irregular menstruation or Amenorrhea, Loss of libido, Hirsutism, Vaginal dryness. → measure serum Prolactin level.
Key 79	Remember that in Pheochromocytoma, before the surgical removal of the adrenal tumour, the patient needs to be given alpha-blockers (e.g. phenoxybenzamine) initially, followed by beta-blocker in order to stabilize the hypertension before the surgery to avoid intraoperative hypertensive crises.
Key 80	Adrenal crisis = (Crisis of Adrenal Insufficiency) = (Crisis of Addison's) = (Very low levels of Cortisol and Aldosterone) - It can occur in a patient with known Addison's disease after *infection*, trauma or surgery. - The commonest cause is *sudden cessation* of exogenous steroids intake (prolonged steroid therapy) = Iatrogenic.

- Features: ill patient with *Hyponatremia*, *Hypotension*, *Hypoglycemia* and *Hyperkalemia*. He might be *tachycardic* and *unconscious*.

- How to manage?

1) Give IV steroids (e.g., 100 mg IV Hydrocortisone), initially.

2) Give IV NS.

3) Cardiac and electrolyte monitoring (as the patient is hyperkalemic).

4) If the precipitating cause of the adrenal crisis is infection (high body temperature) → Give broad spectrum Antibiotics.

5) Correct the hypoglycemia by giving IV hydrocortisone in 5% glucose IV infusion.

Key 81

Quick Notes on Thyroid Nodule First-Step Management:

In any thyroid nodule that is ≥ 1 cm in size

→ Refer to Endocrinology for U/S and FNAC (Fine Needle Aspiration).

Notes:

• If the patient is at the GP clinic, and (refer to endocrinology) is among the option, pick it!

• If the question asks about the ''Initial'' step → Thyroid Ultrasound.

• If the question asks about the most appropriate step → FNAC.

	So, it is U/S followed by FNAC.
Key 82	In DKA, the first step is → IV Normal Saline (0.9% NaCl) followed by IV continuous infusion of regular insulin at 0.1 U/Kg/hour. *Note, the insulin is given as IV infusion NOT Subcutaneous*. Why resuscitation with IV fluid? → Most patients with DKA have already lost around 5 Litres of body fluid!
Key 83	1ry Adrenal insufficiency (Addison's disease) → low *Cortisol and aldosterone* A patient with postural hypotension, weakness, LETHARGY, nausea, vomiting, hyperpigmentation skin and MM. The commonest cause in the UK → Autoimmune. The commonest cause Worldwide → infection (TB). Hypotension, Hyponatremia, Hypoglycemia. The only hyper is K+ (Hyperkalemia) and Hyperpigmentation + Metabolic Acidosis.

	In Addison's disease (1ry): ↑ ACTH → Hyperpigmentation ↓ Aldosterone → Hyponatremia and Hyperkalemia ↓ Cortisol→ postural hypotension and Hypoglycemia. N.B. Suspect Adrenal insufficiency if: N, V, Abd pain + Postural Hypotension.
Key 84	Multiple Myeloma with Hypercalcemia (MM can cause hypercalcemia) - Hypercalcemia picture: • Neuro → lethargy, Confusion, Depression. • GIT → Constipation. • Renal → polyuria (increased urination), Polydipsia (Thirst). • CVS → ECG: Short QT interval. - Causes of hypercalcemia: √ 1ry hyperparathyroidism. √ Multiple Myeloma. √ Sarcoidosis. √ SCC of lung. √ Breast, prostate cancer metastases to bone.

	- Management of Hypercalcemia: • Initially → IV fluid (NS) • Then, Bisphosphonates e.g. (Pamidronate, Zoledronate infusion)
Key 85	**Drug-induced hepatitis** • Co-amoxiclav (Amoxicillin + *clavulanic acid*) can cause hepatitis especially in people with deteriorated liver functions such as in chronic alcoholics. • Clavulanic acid is highly toxic to liver. If the patient already has risk factors for hepatic impairment such as Chronic alcoholism, hepatic excretion of clavulanic acid will be impaired, leading to *cholestasis* (Jaundice and Dark Urine) ''high bilirubin'' and drug-induced hepatitis (incredibly high ALT, AST, ALP). - N.B. drugs that can cause hepatic cholestasis: *Co-amoxiclav*, *flucloxacillin*, *steroids*, *Sulphonylureas*…etc. - N.B. In Alcoholic hepatitis, *AST > ALT*.
Key 86	Tiredness, lethargy, weight gain, intolerance to cold, bradycardia → classical manifestations of Hypothyroidism.

Key 87	The initial step for the management of hypercalcemia → IV fluid. N.B. hypertension can occur due to hypercalcemia. This does not contraindicate IV fluid as an initial step for hypercalcemia.
Key 88	Abdominal pain + Vomiting + HypOtension + Hyperpigmentation (especially on Buccal mucosa, palmar creases, lips) → Addison's disease = Primary Adrenal Insufficiency.
Key 89	A footballer suddenly collapsed when he was playing → Check capillary blood glucose (using glucose oxidase strip) before doing CT or other Ix.
Key 90	The anti-hypertensive agent that causes Hyperkalemia → ACE inhibitors (e.g., Ramipril). :: **Mnemonic** :: Side effects of ACEI = A: Angioedema, C: Cough, E: Electrolyte (K+),

	I: Increased potassium (Hyperkalemia) • N.B. *Spironolactone* (potassium sparing diuretics) can also increase potassium (hyperkalemia). • N.B. *Thiazides* (e.g. Bendroflumethiazide) can cause Hypokalemia, Hyponatremia, Hyperglycemia and Hyperuricemia (Gout: high uric acid) and metabolic alkalosis.
Key 91	Persistent Hypertension that does not respond to treatment + HypOkalemia → Think of Conn's disease (Hyperaldosteronism). Na^+ is either normal or upper normal **Rx**: Start with aldosterone antagonist (e.g. *Spironolactone*), If not useful → Proceed to surgery (*Adrenalectomy*).
Key 92	A patient (e.g. Post-op) has MILD hyponatremia + Mild Hyperkalemia → IV 0.9% Normal Saline (NaCl) infusion. √ IV NS would raise the sodium to normal. It would also correct the slight increase in the potassium.

	√ No need for insulin and glucose if the hyperkalemia is slightly raised (5-5.5). Furthermore, giving insulin with glucose would not correct the hyponatremia. Thus, IV fluid 0.9% sodium chloride is needed.
Key 93	**Remember**: ◙ Small cell lung cancer → High ADH → *SIADH* → ''dilutional'' Hyponatremia (Due to Fluid Retention), Hypokalemia. (Patient may present with frequent falls and confusion). ◙ Small cell lung cancer can also cause High ACTH → (*Cushing*). ◙ SCC of bronchus (lung) → PTH like molecules → *Hypercalcemia*. PTH: Parathyroid hormone
Key 94	Again, Again and Again: The initial step of the management of Hypercalcemia is → IV fluids (0.9% NaCl). Followed by → Bisphosphonates e.g. (Pamidronate, Zoledronate infusion)

Key 95	**Autonomic Neuropathy:** • It affects both sympathetic and parasympathetic branches (Autonomic Nervous System). • Causes to know: *Diabetes*, Alcohol, Aging. • Manifestations: Sweating, Incontinence, *Diarrhea* or Constipation, impotence, postural hypotension. • Suspect it in DM patient with persistent Diarrhea. - N.B. *Metformin* (Biguanide) can cause *Diarrhea* as well!
Key 96	Hypothyroidism Signs: Cold peripheries, hair loss, dry coarse skin, bradycardia, weight gain.
Key 97	**Notes:** • Post-op Hyperglycemia (due to stress) → high cortisol → High glucose (It usually does not last for more than 3 days). Thus, suspect DM if prolonged hyperglycemia even if after surgery or stress. • HbA1C reflects the blood glucose levels in the previous 3 months (as RBCs live for almost 3 months).

	So, in this case (Post-op), glycosylated Hb (HbA1C) would be helpful to differentiate post-op hyperglycemia and DM. • If asked about a Follow Up investigation → Fasting blood glucose. • If HbA1C is high (above 48), then it is DM and NOT stress hyperglycemia. • Metformin is the first line hypoglycemic agent in DM type 2 as long as GFR is above 45.
Key 98	Impaired glucose tolerance is defined as: • Fasting Blood Glucose 5.5-6.9 (below 7) AND • 2-hour oral glucose tolerance 7.8-11
Key 99	Pseudogout can occur with hypothyroidism. (Remember this association)! - The *knee* is the commonest site for pseudogout but it can also affect wrist, ankle, shoulder. - Pseudogout pathognomonic feature: → Aspiration of synovial fluid → +ve Birefringent Crystals Pseudogout → Positive birefringent crystals.

Hypothyroidism can be associated with:

√ Pseudogout.

√ Amenorrhea/ Oligomenorrhea.

√ Hyperprolactinemia (↑ Prolactin).

√ Autoimmune disease e.g. Addison's, pernicious anemia, vitiligo, DM-1.

(Autoimmune hypothyroidism = hashimoto)

For Your Knowledge:

Gout VS Pseudogout

	Gout	Pseudogout
Joint involvement	Smaller joints	Larger joints
Pain	Intense	Moderate
Joint characteristic	Inflammed	Swollen
Typical characteristic	Hyperuricemia	Chondrocalcinosis
Synovial fluid	Uric acid crystals (negative birefringent crystals, needle-like shape)	Calcium pyrophosphate crystals (positive brefringent crystals, rhomboid-shaped)

Key 100	Hyperprolactinemia can occur with Hypothyroidism (Remember this association)! • *Hyperprolactinemia: Galactorrhea, irregular menstruation, loss of libido.* • *Hypothyroidism: Fatigue, Depression, weight gain, constipation, Myxoedema (can present with change in shoe's size for instance).* • Remember that (*Pseudogout*) and (*Hyperprolactinemia*) can occur in association with Hypothyroidism.
Key 101	Hypoglycemia in an unconscious patient → IV Glucose 10% (Without hydrocortisone)
Key 102	Pituitary Macroadenoma → *Galactorrhea* (Hyperprolactinemia) + Compression on optic chiasma → *Bitemporal hemianopia*.
Key 103	**Hx of SCC of lung + Hypercalcemia** What is the next step? Next step would be → Check serum Parathyroid hormone level. In lung malignancy, serum PTH level would be low → (this allows us to rule out primary/ tertiary hyperparathyroidism)

After that,

Check Alkaline phosphatase.

If high → suspect bone metastasis.

So, in lung cancer, if high Ca^{++} and high ALP → Bone metastasis.

Other points with high corrected Calcium (↑ Ca++):

√ High Corrected Calcium + High *Alkaline Phosphatase*

→ Bone metastasis, or thyrotoxicosis, or Sarcoidosis.

√ High Corrected Calcium + High *Albumin* + High *Urea* → Dehydration.

√ High Corrected Calcium + High serum *calcitonin* → B-cell Lymphoma.

Another way:

- ↑ Ca + ↑ Alkaline phosphatase →

  Bone Metastasis, Thyrotoxicosis or Sarcoidosis.

- ↑ Ca + ↑ Albumin + ↑ Urea → Dehydration.

	• ↑ Ca + ↑ serum Calcitonin ➔ B-cell lymphoma. Remember that: • Normal Ca + Normal Phosphate + Normal ALP ➔ Osteoporosis. • Normal Ca + Normal Phosphate + High ALP ➔ Paget's disease. • Low Ca + Low Phosphate + High ALP ➔ Osteomalacia.
Key 104	Remember that: There are 2 important Hypo associated with Alcoholism: → (↓ Glucose & ↓ K^+) 1) HypoGlycemia 2) HypoKalemia • Chronic Alcohol → Vomiting → Loss of K^+ in the vomitus. • Chronic Alcohol → Vomiting → Loss of hydrochloric acid in the vomitus → Metabolic Alkalosis → Activation of RAAS → Loss of K+ in urine. • (*Do not overthink, it is just chronic alcoholism or Vomiting* *→ leads to HypOkalemia*. Full stop!).

Key 105	Hyperprolactinemia features in females: Galactorrhea, Irregular menstruation or Amenorrhea, Loss of libido, Hirsutism, Vaginal dryness.
Key 106	An elderly + Multiple fractures + T-score of -2.5 or lower → Osteoporosis. • First line management → Bisphosphonates (eg, Alendronate ''Alendronic acid'', Pamidronate, risedronate, Zoledronate). • HRT (Hormonal Replacement Therapy) should not be given as a first line management as it has serious side effects such as *Venous Thromboembolism* (VTE), *Stroke*, *Breast cancer*, *coronary diseases*. *T-Score*: assessed by DEXA scan and reflects Bone Mineral Density (BMD): 1) -1 or higher → Normal 2) Between -1 and -2.5 → Osteopenia 3) -2.5 or lower (e.g. -2.8) → Osteoporosis

Key 107	The prolonged use of steroid followed by sudden cessation of steroids → Adrenal insufficiency (N, V, Abd Pain, Dizziness and falls due to postural hypotension) N.B. Dexamethasone is a steroid used in cases of cerebral edema (e.g. due to glioblastoma, brain metastasis).
Key 108	DKA → Give IV fluids with IV regular insulin continuous infusion (First line)
Key 109	Haloperidol (Typical Antipsychotic) → Blocks Dopamine 2 Receptors → Hyperprolactinemia → Erectile Dysfunction. (as on of the features of high prolactin in men) **Notes:** • So, if a question asks about the Anti-psychotic agent that causes Dizziness and Erectile dysfunction (i.e. hyperprolactinemia) → Haloperidol • Most antipsychotic agents can cause Dizziness.

	• Typical Antipsychotics cause hyperprolactinemia, especially Haloperidol. - Mnemonic: haLOperiDol → Low libido (erectile dysfunction).
Key 110	The Anti-thyroid medication that is effective in cases of Thyroid storm (Thyroid crisis) → Propylthiouracil (PTU). It is also preferred during pre-conception, first trimester and post-partum. • **Thyroid storm:** √ A rare but life-threatening exacerbation of thyrotoxicosis. √ It can be precipitated by infection (e.g. pneumonia). √ It presents with Tachycardia, Palpitation, High body Temperature, Diarrhea, Vomiting, reduced consciousness, Tremors. • **Other useful medicines in thyroid crisis:** - *Beta-blockers* (*Propranolol*) → To control Tachycardia and Tremors. - High dose *steroids* → it inhibits the conversion of T4 to T3. - *Iodine* → it inhibits the release of thyroid hormones. - *Cooling*.

	• N.B. *PTU is preferred over Carbimazole in thyroid crises as PTU inhibits peripheral T4 to T3 conversion while Carbimazole reduces the production of T3 and T4 (slower).*
Key 111	The first line treatment of thyrotoxicosis in general is → Carbimazole *Except* in 2 cases where PTU (Propylthiouracil) is preferred: 1) A woman planning to get pregnant or she is in her first trimester pregnancy or postpartum. 2) Thyroid crisis (Storm). Otherwise, pick Carbimazole as it is used only once daily while PTU is used Twice or three times a day with a higher risk of liver injury. • *N.B. Never use Radioactive iodine if there is Grave's Ophthalmopathy or during pregnancy.*
Key 112	Management of Hypoglycemia in an Unconscious patient: - Best → 1 mg IM Glucagon (especially if IV access is difficult) - IV Glucose, examples: • 75 ml of 20% Glucose IV over 10-15 minutes. OR

	• 50 ml of 10% Glucose over 1-2 minutes. - N.B. Oral glucose preparations should not be attempted in an unconscious patient. - N.B. Glucose-containing gel is absorbed by buccal mucosa and is useful in drowsy patients but NOT in unconscious patients.
Key 113	**Remember that:** √ Gliclazide or Glibenclamide (Sulphonylureas) have high risk of Hypoglycemia. √ Therefore, in a patient who is on metformin and gliclazide and keeps getting dizzy and hypoglycemic attacks: → STOP GLICLAZIDE (Sulphonylureas). "imp" • N.B. The target HbA1C in DM 2 → < 53 (some references say <48)
Key 114	**Remember that:** In *Asymptomatic* DM patient, 2 abnormal results are needed to diagnose DM. e.g., if Fasting blood glucose is ≥ 7, we need to repeat FBG or to order HbA1C to diagnose DM.

	Note, FBG is cheaper and is usually used while HbA1C is more expensive and so it is usually used if there is uncertainty. ** Abnormal results include: FBG ≥ 7, or HbA1c ≥ 48* * Note: Tiredness alone cannot be relied upon as a symptom of DM as it can be due to many other conditions.
Key 115	In a DM patient who is on Metformin and Long acting Insulin, if he suffers from repeated hypoglycemic attacks → Consider: reducing the dose of the long acting insulin or even stopping it. • This might be seen in patients who do not eat well (palliative patients for instance who do not have appetite due to cancer). • In these patients, aggressive control of DM is unsuitable; → thus, reduce the dosage of insulin or withhold it.
Key 116	♠ The normal HbA1C is 42. However, in diabetic patients, the target HbA1C is ≤ 48 mmol/mol. "Some references say ≤ 53"

♠ In a patient with hypothyroidism on levothyroxine, if the TSH is still high and T3 and/or T4 is still low

→ Increase the dose of the Levothyroxine.

♦ NOTE:

Never give Ferrous sulphate + Levothyroxine at the same time!

Iron supplement interferes with Levothyroxine's absorption and thus reduces its effectiveness. Therefore, they should be given at separate times with long intervals.

Key 117

Hypokalemia ($\downarrow K^+$)

◙ Some causes:

√ Vomiting → loss of hydrochloric acid → metabolic alkalosis → $\downarrow K^+$.

√ Chronic Alcoholism.

√ 2 Cs → Cushing's (High cortisol), Conn's (High aldosterone).

√ Renal → Bartter's syndrome (in neonates/children, AR).

◙ Some Features:

√ FAINTING. √ Tiredness. √ Weakness. √ Leg Cramps. √ U wave on ECG.

◙ Management:

The normal serum potassium is 3.5-5 mmol/l

- If K^+ is < 2.5 Or, < 3 with ECG Changes "U wave"

→ IV potassium chloride. (e.g. 40 mmol KCl in 1 L Normal Saline IV infusion)

- If K^+ ≥ 2.5, without ECG changes

→ Oral Potassium Supplements.

♦ Remember to order Magnesium and ABG to exclude Metabolic Alkalosis.

♠ Example:

An old patient who complains of recurrent fainting episodes is found to be hypokalemic (K^+ is 2.7).

→ Give Potassium Supplements.

Key 118

In DKA (Diabetic KetoAciosis)

Q) First immediate management?

IV fluids (0.9%) NaCl followed by IV infusion of regular Insulin

	Q) How Much IV fluid NS? (IMPORTANT) ♦ If Systolic Blood Pressure is < 90 → 0.5 or 1 Litre IV Normal Saline Over 10-15 minutes. "rapid; bolus" ♦ If Systolic Blood Pressure is > 90 → 1 Litre IV Normal Saline Over 1-hour. The difference is the duration. (10-15 min VS 1 hour) depending on SBP. Kindly, remember the link between DKA and SGLT-2 inhibitors (Gliflozin). • SGLT-2 inhibitors (Gliflozin) have an important side effect to remember → Genital infections eg, balanoposthitis (erythema and itchiness on the penis glans and prepuce).
Key 118	2ry amenorrhea (cessation of menstruation for > 6 months after it has been established) + Hx of *stress* or *excessive exercise* or *significantly low BMI* → Think of **hypothalamic amenorrhea**

	• This is because hypothalamic failure occurs in these conditions (stress, excessive sports, very low BMI). • In Hypothalamic Amenorrhea → HIGH PROLACTIN. • In hypothalamic failure → ↓ GnRH (Gonadotropin releasing hormone) → ↓ FSH, ↓ LH (with often subsequent ↓ estrogen). These are either low or at lower normal levels. - **To sum up:** If a lady presents with secondary amenorrhea (i.e. after it has been established i.e., she had menstruation in the past but not anymore) + Hx of stress/ excessive exercise Think → Hypothalamic Amenorrhea.
Key 119	A diabetic patient has gastric cancer. She is on metformin and insulin. She developed hypoglycaemia. What to do? → Reduce the insulin dose. In a DM patient who is on Metformin and Long acting Insulin, if he suffers from repeated hypoglycemic attacks → Consider either *reducing the dose of the long acting insulin or even stop it*.

	• This might be seen in patients who do not eat well (palliative patients for instance who do not have appetite due to cancer). • In these patients, aggressive control of DM is unsuitable; thus, reduce the dosage of insulin or withhold it.
Key 120	**Hypocalcemia (↓ Ca^{++}) management** → give Calcium gluconate first line. **Hypercalcemia (↑ Ca^{++}) management** → give IV fluid normal saline (sodium chloride) first line.
Key 121	◆ A man with Thyrotoxicosis + he is already taking propranolol → Carbimazole ◙ The first line treatment of thyrotoxicosis in general is → Carbimazole Except in 2 cases where PTU (Propylthiouracil) is preferred: 1) A woman planning to get pregnant or she is in her first trimester pregnancy or postpartum. 2) Thyroid crisis (Storm).

	Otherwise, pick Carbimazole as it is used only once daily while PTU is used twice or three times a day with a higher risk of liver injury. • N.B. Never use Radioactive iodine if there is Grave's Ophthalmopathy or during pregnancy. ♦ A woman in first trimester was found to have low TSH (hyperthyroidism) → Propylthiouracil ♦ A postpartum breastfeeding woman presents with palpitations, tachycardia and tremors. Her TSH is low. → Postpartum thyroiditis in the hyperthyroidism phase. → Give Propranolol to manage the symptoms of palpitations and tremors. *Postpartum thyroiditis usually resolves on its own in 1 year after delivery. Therefore, anti-thyroid medications (e.g. carbimazole, propylthiouracil) are not needed. However, in the hypothyroid phase, levothyroxine can be used.* Note: Thyroid peroxidase antibodies are positive in around 80% of postpartum thyroiditis cases.
Key 122	A woman presents with constipation and weight gain. The Likely Dx → Hypothyroidism.

Key 123	T-Score by DEXA scan of – 2.5 or lower (e.g., -2.9) → Osteoporosis → give Bisphosphonate (e.g., alendronate, risedronate, zoledronate).
Key 124	A patient on metformin and gliclazide. He keeps getting dizzy and hypoglycemic attacks → Omit Gliclazide. **Remember that:** Gliclazide or Glibenclamide (Sulphonylureas) have high risk of Hypoglycemia. Therefore, in a patient on metformin and gliclazide who keeps getting dizzy and hypoglycemic attacks → STOP GLICLAZIDE (Sulphonylureas). • N.B. The target HbA1C in DM 2 → ≤ 53 (some references say ≤ 48)
Key 125	A man with High BMI (obese) was found to have a high fasting blood glucose. What should be done? → Repeat the test in weeks. (usually, after 2 weeks). In Asymptomatic people → 2 tests need are needed to confirm DM.

Key 126	A 22 YO female presents complaining of her high weight. She asks for help for her obesity. What should be initially done? → Lifestyle and diet modification.
Key 127	A patient with lung cancer presents with confusion. Among the lab abnormalities, there is serum sodium of 128 (hyponatremia). → SIADH (Syndrome of Inappropriate Antidiuretic Hormone). √ The mainstay Rx → Fluid Restriction. √ If failed → Tolvaptan or Demeclocycline. --- **Remember**: • Small cell cancer of the lung → SIADH & Cushing. • SCC of the lung → Hypercalcemia. --- **Also, remember**: ♦ SIADH: Hyponatremia (low Sodium), Low Serum Osmolality, High Urine Osmolality.

	♦ Diabetes insipidus (DI): Hypernatremia, Low Urine Osmolality, High Serum Osmolality. *(This low urine osmolality in DI increases after giving vasopressin)*
Key 128	A postpartum breastfeeding woman presents with palpitations, tachycardia and tremors. Her TSH is low. → Postpartum thyroiditis in the hyperthyroidism phase. → Give Beta-blockers e.g., Propranolol to manage the symptoms of palpitations and tremors. *Postpartum thyroiditis usually resolves on its own in 1 year after delivery. Therefore, anti-thyroid medications (e.g. carbimazole, propylthiouracil) are not needed. However, in the hypothyroid phase, levothyroxine can be used.* Note: Thyroid peroxidase antibodies are positive in around 80% of postpartum thyroiditis cases.
Key 129	◙ A patient presents with weight loss despite eating well, fine tremors, no neck swelling. Rx → Carbimazole (likely hyperthyroidism). ◙ A pregnant woman in her first trimester presents with weight loss despite eating well, fine tremors, no neck swelling. Rx → Propylthiouracil

	* Propylthiouracil is preferred preconception (before pregnancy if the woman is planning to get pregnant) and in the first trimester and postpartum + in thyroid storm. Otherwise: Carbimazole is preferred. ◙ A postpartum female (delivered 2 months ago) presents with palpitations and tremors. Her TSH is low. → Propranolol (beta blockers) to control symptoms. (Postpartum thyroiditis) *All these 3 cases were asked recently in PLAB 1 exam.*
Key 130	◙ A 55 YO man was found to have high blood glucose post-operatively. A few days later, his glucose was found to be normal → Stress Hyperglycemia.
Key 131	◙ A female presents with Galactorrhea, irregular menstruation, loss of libido. → order Prolactin level. (Likely hyperprolactinemia).
Key 132	A 45 YO female presents with increased thirst and increased urination. Her calcium is 2.9 (normal is 2.1-2.6). Her phosphate is 0.7 (normal is 0.8-1.4). Her parathyroid hormone is 8.4 (normal is 0.8-8.5). The likely Dx → **Primary Hyperparathyroidism**.

PTH → Normal (in 1ry HPT, parathyroid hormone can be normal or high).
Calcium → High (Featured also by the polydipsia and polyuria).
Phosphate → Low

• **Parathyroidectomy** is the most definitive treatment for patients with primary hyperparathyroidism especially symptomatic patients and in those who have osteoporosis or fractures. √

• The most common cause of primary hyperparathyroidism is
→ Parathyroid adenoma, mainly **solitary parathyroid adenoma**.

Hyperparathyroidism	Parathyroid Hormone	Calcium	Phosphate
Primary (Commonest cause is parathyroid adenoma)	Normal or High	HIGH	LOW
Secondary (↑ PTH due to existing hypocalcemia esp. 2ry to CKD)	HIGH	LOW or normal	High or normal
Tertiary	End-Stage Renal Failure PTH, Ca, Ph are high. On U/S → hyperplasia of parathyroid glands.		

	Primary hyperparathyroidism	Secondary hyperparathyroidism	Tertiary hyperparathyroidism
PTH	↑/N	↑	↑↑↑
Ca2+	↑ *	↓/N	↑
P04+	↓	↑/N	↑
Vitamin D	N/↓	↓↓↓	↓/N
Comments	In 85% a solitary parathyroid adenoma is present Important differential diagnosis is FHH Familial Hypocalciuric Hypercalcemia	Causes include: • chronic renal failure • vitamin D deficiency Prolonged Hypocalcemia stimulates the excessive release of PTH	Caused by: • end stage renal failure PLAB KEYS

Key 133

2 Important Points on Congenital Adrenal Hyperplasia (Autosomal Recessive):

◙ (1) It may present in neonates and children with the following features:

- Female → Ambiguous genitalia.
- Male → Penile Enlargement, Hyperpigmentation
- Infant Male → Salt Wasting (due to Aldosterone Deficiency)

→ Vomiting, Weight Loss, Lethargy, Dehydration, ↓Na+, ↑K+

→ (11-ß-Hydroxylase Deficiency)

If this is the stem, we order → Aldosterone level.

◙ (2) In adults:

• Males → No signs, may be hyperpigmentations (due to ↑ melanocyte-stimulating hormone) "not asked in exam before".

• Females → Hirsutism (excessive hair growth in the face, chest, back), Acne, Early pubarche, Oligomenorrhea (due to ↑ 17-hydroxyprogesterone that is converted into androgens; testosterone, androstenedione).

If this is the stem, we order → 17-hydroxyprogesterone.

Also, remember that the commonest form of Congenital Adrenal Hyperplasia is *21 alpha-hydroxylase deficiency*.

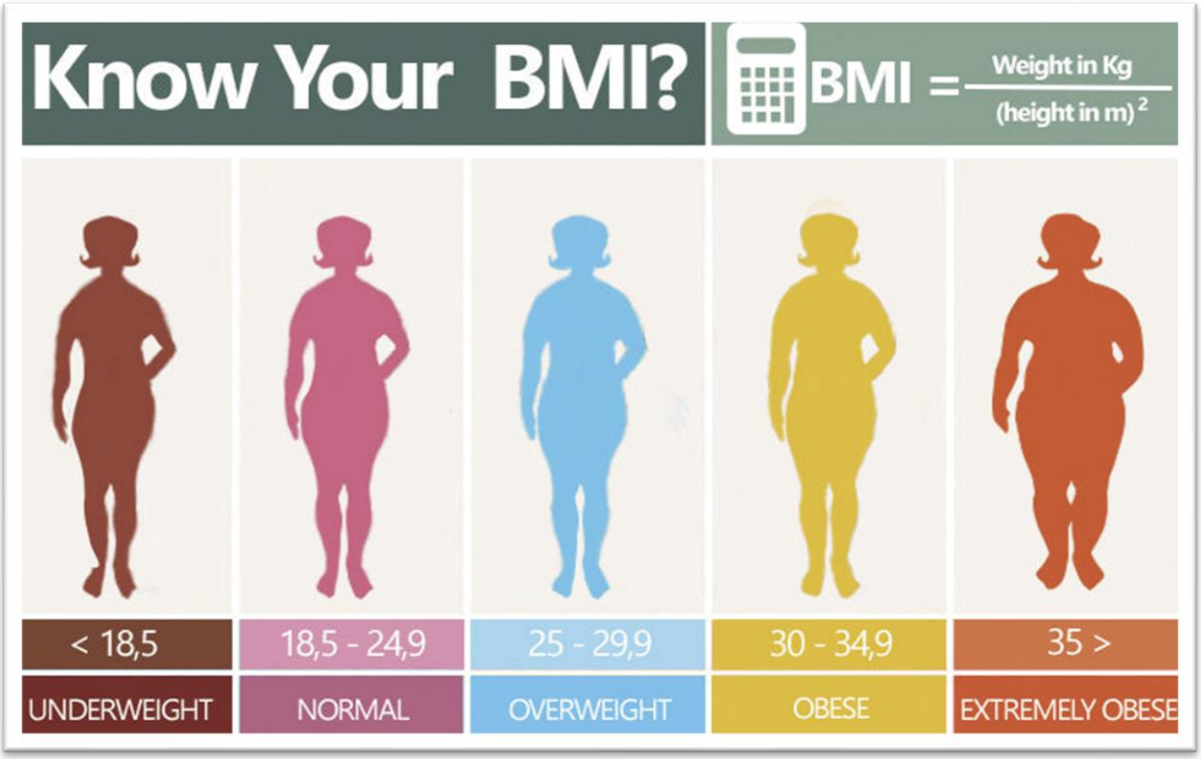
Remember that polycystic ovarian syndrome (PCOS) is different:
◙ Inability to conceive (infertility) + Obesity + Acne + ↑ LH
→ Polycystic ovarian syndrome PCOS → (order pelvis ultrasound)

Example,

A young lady has excessive hair growth on her face and chest. She reached pubarche early at age of 11 years. Her menstrual periods are irregular and infrequent. She also has acne on the face. Her BMI is 23. Her BP is normal.

◙ The likely Dx → Congenital adrenal hyperplasia
(CAH: autosomal recessive: 1:4 risk if both parents are carriers)

◙ The appropriate hormone level to order → 17-hydroxyprogesterone.

	√ This is not Polycystic ovarian syndrome (PCOS). √ Remember, in PCOS, the patient is usually obese which is not the case here (her BMI is 23: normal). Also, in PCOS, LH is high (LH: FSH is ≥ 2:1), which is not given here. 
Key 134	Scenario (1) A 54 YO man known case of DM and HTN on metformin, ramipril and bisoprolol. His blood pressure is 135/88 and his BMI is 30 kg/m2. His labs: Urea 7 (Normal: 2-7) ▌Creatinine 140 (Normal: 70-150) eGFR 65 (Normal >90) ▌HbA1c 52 (Target: < 48)

Remember these Important points:

♦ If the patient has new Dx of DM-2, advice firstly for lifestyle modifications. If after this, his HbA1c is still > 48 → start 1 hypoglycemic (e.g., metformin).

♦ If the patient is already on Metformin, and his HbA1c is high but < 58
→ Advice for lifestyle modifications.

♦ If the patient is already on Metformin, and his HbA1c is ≥ 58
→ Add another hypoglycemic agent.

The patient in this stem belongs to the second point. He is already on metformin but still a bit hyperglycemic. As his HbA1c is <58, the answer would be
→ continue the same management but encourage lifestyle and diet changes.

◙ So, when to advise for lifestyle modifications?

√ Newly diagnosed patient with DM-2. Or:

√ Already on metformin and his HbA1c high but still < 58 (not very high).

◙ When to consider adding another hypoglycemic agent?

√ If he is on metformin but his HbA1c is > 58.

Scenario (2)

A 54 YO lorry driver man, known case of DM and HTN on metformin, ramipril and bisoprolol. His blood pressure is 135/88 and his BMI is 30 kg/m2. His labs:

Urea 7 (Normal: 2-7) ▌Creatinine 140 (Normal: 70-150)

eGFR 50 (Normal >90) ▌HbA1c 58 (Target: < 48)

Since his HbA1c is 58, he needs an additional hypoglycemic medication.

√ Sulphonylureas is contraindicated as it can cause weight gain and hypoglycemia. This man is quite obese and is a lorry driver "hypoglycemia is dangerous here".

√ SGLT-2 inhibitors (e.g., Gliflozins) should be avoided if eGFR < 60.

√ Insulin is not indicated unless 3 drugs are required. Also, it is not ideal for lorry drivers.

The safest option here is → Gliptins "no effect on BMI, safe in renal impairment".

Scenario (3)

A 54 YO ambulance driver man, known case of DM and HTN on metformin, ramipril and bisoprolol. His blood pressure is 135/88 and his BMI is 32 kg/m2. His labs:

Urea 7 (Normal: 2-7) ▌Creatinine 140 (Normal: 70-150)

eGFR 70 (Normal >90) ▌HbA1c 58 (Target: < 48)

The patient is a smoker, and exercises only 30 minutes a week

→ Reinforce advice about diet and lifestyle.

(He is a smoker, and with little exercise, he needs to stop smoking and to exercise more. NICE advise for 150 minutes/ week of moderate intensity physical activity e.g. cycling for 30 minutes a day, 5 days a week).

√ If this patient has been already exercising well and his HbA1c is still 58, the next option would be SGLT-2 inhibitors as they can reduce weight (his BMI is high) compared to gliptins which are neutral to weight.

√ SGLT-2 inhibitors should be avoided if eGFR is < 60. Here it is 70.

√ Sulphonylureas are contraindicated in lorry/ ambulance drivers as they can cause hypoglycemia. They also cause weight gain (here, he is obese).

◙ Scenario (4)

A man with BMI of 35, HBA1c of 56, no hyperglycaemic symptoms, already started lifestyle modifications 3months ago, next appropriate medication?

a. metformin

b. sitagliptin

c. insulin

d. glimepiride

e. lifestyle modification

√ Since the lifestyle modification has been started but his HbA1C is still above 48, we need to commence 1 hypoglycemic.

√ Since he is obese, with no severe renal impairment, metformin is the first drug to start with.

Important Mnemonics for Hypoglycemics

- With bad kidneys (*GFR < 30*), do not use MS (Metformin, Sulphonylureas).
- The heart has 4 chambers, so with HF (and pancreatitis), do not use DDP4 inhibitors (gliptins).
- Also, the Pie (Pioglitazone) comes with the die (Risk of bladder cancer). So, Pioglitazone has a risk for Bladder Cancer. Pioglitazone is also contraindicated in HF.
- Hypoglycemics that cause weight gain (↑) are SPR (Sulphonylureas, Pioglitazone, Repaglinide). The rest cause weight loss (↓) except DDP4 inhibitor Which has no effect on the weight.

	• SPR without the P have risk of hypoglycemia: Sulphonylureas and Repaglinide. • SGLT-2 inhibitors (Gliflozin) have increased risk for euglycemic DKA. • SGLT-2 inhibitors (Gliflozin) have an important side effect to remember → Genital infections eg, balanoposthitis (erythema and itchiness on the penis glans and prepuce).
Key 135	◙ **Scenario (1):** A woman with 6-month history of amenorrhea. Pregnancy test is negative. She is physically fit and is a long-distance runner. Estrogen: 80, FSH: 11, Prolactin: 600 A hypothalamic amenorrhea B pcos C post pill amenorrhea D pof E prolactinoma 2ry amenorrhea (cessation of menstruation for > 6 months after it has been established) that occurs with stress or excessive exercise or significantly low BMI → Think of hypothalamic amenorrhea - This is because hypothalamic failure occurs in these conditions. - In Hypothalamic Amenorrhea→ HIGH PROLACTIN.

	◙ Scenario (2): A 37 YO woman has stopped taking COCP 6 months ago and she has been amenorrheic since then. Her investigations are as follows: Pregnancy test: -ve. FSH: 25 (upper normal). LH: 15 (normal). Prolactin: 550 (the normal is below 400). Liver and kidney function tests are normal. BMI: 24 What is the likely cause for her amenorrhea? A Hypothalamic amenorrhea B pcos C post pill amenorrhea D premature ovarian failure E prolactinoma • In post pill amenorrhea: FSH, LH, Prolactin are normal or mildly elevated. • PCOS would have high BMI, high LH, other features of PCOS. Needs U/S. • Premature ovarian failure would need 2 separate result of FSH > 25. • Prolactinoma would be suspected if prolactin is significantly high (>1000). • Hypothalamic amenorrhea: all ↓ (estrogen, BMI, LH, FSH). Hx of sport/stress.
Key 136	79-year-old woman presents with increased thirst, polyuria, constipation of two weeks. There is increasing confusion over the last 3 days. She had left mastectomy for breast Ca. She is taking fluoxetine. Temp is 36.9, HR 100,

	reduced skin turgor. No papilloedema or focal neurological signs. Urinalysis showed trace ketones. What is the likely cause? A) Cerebral metastasis B) DKA C) hypercalcemia D) hyponatremia E) fluoxetine overdose Some features of hypercalcemia such as: • Neuro → lethargy, Confusion, Depression. • GIT → Constipation, Nausea, Vomiting • Renal → polyuria (increased urination), Polydipsia (Thirst). • CVS → ECG: Short QT interval. Bone metastasis is common in breast cancer → ↑ Ca^{++}
Key 137	A 64 yr old presenting with confusion. He has had cough for 1 month with weight loss. Serum Ca: 3.4 (Normal 2.1-2.6) Most appropriate initial management? a) IV 0.9% saline infusion b) alendronate infusion c) dialysis d) resection of tumor The initial management of hypercalcemia → IV fluid NS.

	Then → Bisphosphonates (eg, alendronate, pamidronate). SCC of bronchus (lung) → PTH like molecules → *Hypercalcemia*.
Key 138	A man with BMI of 31 and HbA1c of 56 mmol/l, 3 months of lifestyle modification was tried yet HbA1c is still above 53, what is next important management? a) Metformin b) Insulin c) Gliclazide d) Pioglitazone e) glibenclamide He is obese, remember: • Hypoglycemics that cause weight gain (↑) are SPR (Sulphonylureas, Pioglitazone, Repaglinide). The rest cause weight loss (↓) except DDP4 inhibitor Which has no effect on the weight. • Also, the first line hypoglycemic in DM 2 is metformin as log as there is no marked renal impairment. *Important Mnemonics for Hypoglycemics* • With bad kidneys (*GFR < 30*), do not use MS (Metformin, Sulphonylureas). • The heart has 4 chambers, so with HF (and pancreatitis), do not use DDP4 inhibitors (gliptins).

	• Also, the Pie (Pioglitazone) comes with the die (Risk of bladder cancer). So, Pioglitazone has a risk for Bladder Cancer. Pioglitazone is also contraindicated in HF. • Hypoglycemics that cause weight gain (↑) are SPR (Sulphonylureas, Pioglitazone, Repaglinide). The rest cause weight loss (↓) except DDP4 inhibitor Which has no effect on the weight. • SPR without the P have risk of hypoglycemia: Sulphonylureas and Repaglinide. • SGLT-2 inhibitors (Gliflozin) have increased risk for euglycemic DKA. • SGLT-2 inhibitors (Gliflozin) have an important side effect to remember → Genital infections eg, balanoposthitis (erythema and itchiness on the penis glans and prepuce).
Key 139	33yr old woman with weight loss of 6kg, has fine tremors. TSH – D–creased. T3 and T4 are Increased. What to give? A. Carbimazole B. Propylthiouracil C. Prednisolone D. Hydrocortisone √ The Rx of Hyperthyroidism generally is Carbimazole. √ Propylthiouracil is used if the patient is a woman who intends to get pregnant, or if she is already pregnant in the first trimester, or postpartum. √ Propylthiouracil is also preferred during (thyroid storm).

Key 140

A diabetic man was found unconscious. His blood glucose reads 1.7. He does not have IV access. What should be done?

→ Place IV line and give 75 ml of 20% glucose IV.

If blood sugar is below 4 → It is hypoglycemia

√ If unconscious:

- 75 ml of 20% Glucose IV over 10-15 minutes. OR
- 50 ml of 10% Glucose over 1-2 minutes. OR
- 1 mg glucagon IM or SC.

Key 142

Quick Important Comparison by Plab1Keys.com

Condition	Hormonal defects	Main features	Investigations
Cushing	↑ cortisol	Hyperglycemia, hypertension, hypokalemia Others: striae, moon face, obesity, liability to infections, cardiac hypertrophy. ♀ : Amenorrhea, dark facial hair.	• Screening: 24-hour free cortisol in urine. • To establish Dx: low dose overnight dexamethasone suppression test. • To localise the problem: high dose dexamethasone suppression test

	Addison's (1ry adrenal insufficiency)	↓ cortisol, ↓ aldosterone	Hypoglycemia, Hyponatremia, Hypotension, Hyperkalemia, skin hyperpigmentation, others: weakness, nausea, vomiting, abd. Pain, metabolic acidosis	ACTH stimulation test (short Synacthen test).
	Pheochromocytoma	↑ catecholamine (epinephrine, norepinephr.)	PHE: Palpitations, Hypertension, Headache, Flushing, Episodes.	24 hours collection of urine metanephrines
	Conn's (1ry hyperaldost-eronism)	↑ aldosterone	Hypertension, Hypokalemia (e.g. muscle weakness), normal or upper normal Na+, (refractory HTN), metabolic alkalosis Others: weakness, lethargy, headache.	• Plasma aldosterone/renin ratio is the first-line • Following this →, high-resolution CT abdomen and adrenal vein sampling. [Plab1keys.com]

Key 143

Bartter's Syndrome

◙ Usually autosomal recessive.

◙ Severe hypokalaemia. (↓↓↓ K^+).

◙ Due to defective chloride absorption at the Na+ K+ 2Cl- cotransporter (NKCC2) in the ascending loop of Henle.

◙ Careful! It is associated with normotension

(Unlike other endocrine causes of hypokalaemia such as Conn's, Cushing's and Liddle's syndrome that are associated with hypertension).

√ As Loop diuretics work by inhibiting NKCC2, think of Bartter's syndrome as like taking large doses of furosemide.

◙ Features:

• Usually presents in childhood (Classic Bartter's), e.g., Failure to thrive. Another major type is the neonatal Bartter's syndrome "seen between the gestational week 24-30 with excess amniotic fluid (polyhydramnios). After birth, excessive polyuria and polydipsia with tendency to dehydration.

• Polyuria, polydipsia (think of it as like taking large doses of loop diuretics).

• Hypokalaemia (↓ K+).

• Normotension (Normal BP). Or sometimes low BP but not high!

• Weakness.

◙ Treatment (Reading):

√ Sodium, chloride and potassium supplementation is necessary.

√ Spironolactone can be also used to reduce potassium loss.

√ Free and unqualified access to water is necessary to prevent dehydration, as patients maintain an appropriate thirst response.

√ In severe cases where supplementation alone cannot maintain biochemical homeostasis, nonsteroidal anti-inflammatory drugs (NSAIDs) can be used to reduce glomerular filtration, and can be very useful, although may cause gastric irritation and should be administered alongside stomach acid suppression therapies.

√ Angiotensin-converting enzyme (ACE) inhibitors can also be used to reduce glomerular filtration rate.

Surveillance renal ultrasound should be employed to monitor for the development of nephrocalcinosis which is a common complication.

Remember,

Important causes of Hypokalemia to know → 2 C + B

1) Conn's (1ry hyperaldosteronism): but with Hypertension.

2) Cushing (excess cortisol): but with Hypertension.

	3) Bartter's: but with normal BP "Normotension" or sometimes low BP. **Do not get confused!** In Congenital Adrenal Hyperplasia (Also autosomal recessive): ◙ Cortisol Deficiency ± Aldosterone Deficiency ± Androgen Excess. ◙ Vomiting, Weight Loss, Lethargy, Dehydration, ↓Na+, ↑K+
Key 144	In patients with Hx of malignancy (e.g. Lung cancer, breast cancer), if the patient develops hypercalcemia (↑ Ca++), the next step would be to order ALP (Alkaline phosphatase). This is to confirm/ exclude metastasis. **Remember**: ◙ High Corrected Calcium + High *Alkaline Phosphatase* → Bone metastasis, or thyrotoxicosis, or Sarcoidosis. ◙ High Corrected Calcium + High *Albumin* + High *Urea* → Dehydration. ◙ High Corrected Calcium + High serum *calcitonin* → B-cell Lymphoma.

Key 145

Important side effects of different types of diuretics:

Loop diuretic e.g., Furosemide bumetanide	Thiazide-like diuretics e.g., Bendroflumethiazide Indapamide	Potassium-sparing diuretics e.g., Spironolactone eplerenone
Hyponatremia	Hyponatremia	Hyponatremia
Hypokalemia	Hypokalemia	HypeRkalemia
Gout (hyperuricemia)	Gout (hyperuricemia)	Gynecomastia
	Postural Hypotension	
	Hyperglycemia (impaired glucose tolerance)	

◙ Remember that,

ACE inhibitors (e.g. ramipril, enalapril) can cause:

Angioedema, Dry cough, Hyperkalemia (↑ K^+).

	◙ Other important reasons for hyperkalemia (↑ K^+) to remember: √ ACE inhibitors (e.g. ramipril, captopril, enalapril). √ Potassium-sparing diuretics (e.g. spironolactone). √ Adrenal insufficiency (Addison's disease).
Key 146	A 42 YO man presents with polyuria, polydipsia and raised red dots on his glans penis. The most imp. Ix to diagnose → Fasting blood glucose. This patient has Fungal balanitis 2ry to DM. Diabetic patients have reduced immunity → prone to fungal infections.
Key 147	A 60 YO woman presents with the followings: √ Confusion. √ Weakness. √ Pains and aches. √ Polyuria and Polydipsia. √ Hx of renal calculi. √ High parathyroid hormone level. √ High serum calcium.

√ Low serum phosphate.

√ Normal eGFR.

Interpretation and most likely diagnosis:

↑ or normal PTH, ↑ Ca++, ↓ Ph → think 1ry hyperparathyroidism.

√ This woman likely has primary hyperparathyroidism.

√ The commonest cause of it is → Parathyroid Adenoma.

√ The features presented are due to Hypercalcemia (bone aches, confusion, renal calculi, excessive thirsty and urination).

√ Note that in 2ry hyperparathyroidism, the Ca++ would be low, and also the eGFR would not be normal.

Hyperparathyroidism	Parathyroid Hormone	Calcium	Phosphate
Primary (Commonest cause is parathyroid adenoma)	Normal or High	HIGH	LOW
Secondary (↑ PTH due to existing hypocalcemia esp. 2ry to CKD)	HIGH	LOW or normal	High or normal
Tertiary	End-Stage Renal Failure		

Key 148	A 60 YO woman presents with the Followings: √ Hypertension √ Weight gain √ Proximal muscle weakness (Cannot abduct shoulder, flex hip). √ Easy bruising √ Hypernatremia and hypokalemia ◙ The best initial test to establish the Dx → 1 mg (low-dose) = Overnight Dexamethasone Suppression test. ◙ The likely Dx is → Cushing.
Key 149	A patient with hyperthyroidism and a swelling of the right lobe of the thyroid gland. Isotope scan shows → increased radioactive iodine uptake in a solitary region of the right lobe of the thyroid gland while it is low in the rest. Both TPO (thyroid peroxidase) antibody and TSH receptor antibody are negative. What is the likely Dx?

	√ TPO antibody and TSH receptor antibody are negative → NOT Graves. √ Increased radioactive iodine uptake in an isolated region of the right lobe → Solitary nodular goitre.
Key 150	◙ Although DM type 1 is usually diagnosed at a young age (juvenile-onset), it can still present in adulthood. This is known as LADA "Late Autoimmune Diabetes of the Adults". It is a variant of DM type 1 but with slow progression and thus is presented in adults. ◙ DM-1 can be associated with other autoimmune conditions such as vitiligo and Grave's disease. ◙ Glutamic Acid Decarboxylase (GAD) Antibodies Test is helpful in differentiating DM type 1 from DM types 2. *√ Side note: C-peptide test is useful in diagnosing Insulinoma.* *An insulinoma causes the pancreas to release too much insulin, which causes blood sugar levels to drop (hypoglycemia). A person with an insulinoma will have a high level of C-peptide in the blood when they have a high level of insulin.*

Key 151	MODY (Maturity Onset Diabetes in the Young). - *DM < 25 Y/O* - *Strong FHx* (2 generations) - Mild Hyperglycemia - No need for insulin initially. Responds to Sulphonylureas. √ The most appropriate next step in Dx is to send for genetic counselling. √ For Rx → Refer to secondary care diabetic clinic + Lifestyle advice.
Key 152	Patients with Addison disease who are already on hydrocortisone need to DOUBLE the dose of hydrocortisone during their sick days (e.g. Flu, COVID 19…etc). If Addison crisis is suspected (e.g., worsening confusion and abdominal pain, feeling very thirsty, dizzy), admit for IV hydrocortisone.
Key 153	A 10 YO boy is admitted for the treatment of meningitis. He was found to have low serum sodium. What is the reason for this hyponatremia?

	→ SIADH 2ry to meningitis. Remember, of the important causes of SIADH: meningitis and small cell lung cancer.
Key 154	**Hypopituitarism:** √ Hypopituitarism is the decreased (hypo) secretion of one or more of the eight hormones normally produced by the pituitary gland at the base of the brain. √ If there is decreased secretion of one specific pituitary hormone, the condition is known as selective hypopituitarism. √ If there is decreased secretion of most or all pituitary hormones, the term panhypopituitarism (pan meaning "all") is used. ◙ The hormones released by the pituitary gland: • Anterior pituitary: • Growth hormone (GH) • Adrenocorticotrophic hormone (ACTH) • Thyroid-stimulating hormone (TSH) • Luteinising hormone (LH) • Follicle-stimulating hormone (FSH) • Prolactin (PRL)

- Posterior pituitary:
  - Antidiuretic hormone (ADH).
  - Oxytocin.

- Intermediate zone: Melanocyte-stimulating hormone (MSH)

Pituitary lobe	Associated hormones	Effect
Anterior	Growth hormone (GH)	Promotes growth of body tissues
Anterior	Prolactin (PRL)	Promotes milk production from mammary glands
Anterior	Thyroid-stimulating hormone (TSH)	Stimulates thyroid hormone release from thyroid
Anterior	Adrenocorticotropic hormone (ACTH)	Stimulates hormone release by adrenal cortex
Anterior	Follicle-stimulating hormone (FSH)	Stimulates gamete production in gonads
Anterior	Luteinizing hormone (LH)	Stimulates androgen production by gonads
Posterior	Antidiuretic hormone (ADH)	Stimulates water reabsorption by kidneys
Posterior	Oxytocin	Stimulates uterine contractions during childbirth
Intermediate zone	Melanocyte-stimulating hormone	Stimulates melanin formation in melanocytes

◙ Causes of Hypopituitarism:

√ Pituitary adenoma “most common”.

√ Other tumours “e.g., meningioma, glioma”.

√ Inflammatory disease “e.g., TB, meningitis, sarcoidosis”.

√ Trauma.

√ Stroke.

√ Radiotherapy.

√ Sheehan's syndrome (due to a major postpartum hemorrhage leading to pituitary ischemia and necrosis and featured early by failure to lactate, amenorrhea and then lethargy, weight gain …etc). √

◙ Clinical features of hypopituitarism:

Examples:

• ↓ GH → "usually no symptoms in adults apart from loss of muscle mass and central obesity sometimes".

• ↓ LH, FSH → Amenorrhea, oligomenorrhea, infertility

"In men → erectile dysfunction"

• ↓ TSH → Fatigue, cold intolerance, weight gain "2ry hypothyroidism symptoms where TSH and T4 are both low".

• ↓ ACTH → Hyponatremia "↓ serum Na+", hypotension, weight loss, skin pigmentation changes".

• ↓ Prolactin → absent lactation "rare. But seen in Sheehan's syndrome".

◙ Rx → usually replacing hormones. Most hormones controlled by the secretions of the pituitary can be replaced by tablets or injections.

◙ Example:

A 34 YO woman has fatigue, low mood and irregular menstrual cycles (only 3 menstrual cycles over the past year). She has been trying to conceive "to get pregnant" for the past 2 years but failed. Her blood labs are as follows:

LH and FSH: low

TSH: low

Free T4: low

Serum sodium: low

Serum potassium: normal.

The likely Dx → Hypopituitarism.

Notes:

√ Her low serum sodium is due to low ACTH.

√ Her low LH and FSH have cause oligomenorrhea and infertility.

√ Low TSH and T4 means 2ry hypothyroidism "thus, fatigue".

In primary hypothyroidism, TSH would be high and T4 would be low.

Key 155

ALL unexplained thyroid lumps "swellings" should be referred urgently to an endocrinologist to rule out thyroid carcinoma. Imp. √

"Even if no clues of thyroid cancer such as weight loss or hoarseness of voice. Urgent referral to an endocrinologist for the possibility of thyroid cancer should be made"

NICE suspected Head and Neck cancer pathway referral criteria (for an appointment within 2 weeks):

◙ Laryngeal cancer

- Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for laryngeal cancer in people aged 45 and over with:
  - persistent unexplained hoarseness or
  - an unexplained lump in the neck

◙ Oral cancer

- Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for oral cancer in people with either:
  - unexplained ulceration in the oral cavity lasting for more than 3 weeks or
  - a persistent and unexplained lump in the neck.
- Consider an urgent referral (for an appointment within 2 weeks) for assessment for possible oral cancer by a dentist in people who have either:
  - a lump on the lip or in the oral cavity or

	○ a red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia. ◙ **Thyroid cancer** • Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for thyroid cancer in people with an unexplained thyroid lump.
Key 156	**Subclinical Hypothyroidism** TSH is high, BUT free T3 and T4 are normal. ◙ Next step? → Repeat TSH in 3 to 6 months. ◙ What next? • If TSH is still high but (< 10) in both tests "with 3 months apart": √ Asymptomatic patient → No Rx required. √ Symptomatic but ≥ 65 YO → No Rx is required (fear of AF). √ Symptomatic and < 65 YO → Consider levothyroxine.

• If TSH is still high (> 10) in both tests "with 3 months apart":

√ Consider levothyroxine.

(Normal TSH range is 0.5-5.7 mU/L).

Example (1):

A 45 YO woman has been tired for the past few months. Her labs show:

Normal FBC.

TSH is 13 (normal: 0.5-5.7).

Free T4 is 11 (normal: 9-18).

What is the most appropriate next step?

→ Repeat TSH in 3-6 months.

What if she still has elevated TSH > 10 and still having tiredness?

→ Consider levothyroxine (2 TSH tests > 10, symptomatic, <65 YO).

Example (2):

A 66 YO woman has been tired for the past few months. Her labs show:

Normal FBC.

TSH is 13 (normal: 0.5-5.7).

Free T4 is 11 (normal: 9-18).

3 months later, TSH is repeated and found to be 8. She is still having fatigue. What should be done?

→ No Rx required (although she is symptomatic, her second TSH is still high but below 10, she is >65 YO. Thus, no Rx is required).

Example (3):

A 50 YO has incidental blood results showing:

Normal FBC.

TSH 8 (normal: 0.5-5.7).

Free T4 is 11 (normal: 9-18).

3 months later, TSH is repeated and found to be 9, and free T4 is 12.

Her thyroid antibodies test is negative. What should be done?

→ No Rx required (Reassure).

Both TSH tests with 3 months apart are elevated (however still <10)

She is asymptomatic

→ No Rx required.

Example (4):

A 25 YO woman presents with fatigue, tiredness and dry skin. Her labs:

Normal FBC.

TSH 9.8 (normal: 0.5-5.7).

Free T4 is 11 (normal: 9-18).

3 months later, TSH is repeated and found to be 8.5, and free T4 is 14.

She has no palpable goitre. She is trying to conceive.

What should be done?

→ Consider levothyroxine.

√ TSH is high, T4 is normal → subclinical thyroiditis.

	√ Both TSH (with 3 months apart) are high but below 10. She is symptomatic, and trying to conceive. She is <65 YO → Consider starting levothyroxine. --- **Note:** √ Subclinical hypothyroidism alone → Manage in primary care. √ Subclinical hypothyroidism + She is planning to get pregnant → **Refer to an endocrinologist**.
Key 157	A 30 YO man has extreme thirst and polyuria (3.5 Litres a day) over the last month. His labs are normal except a mild hypernatremia. • Suspect → Diabetes Insipidus (DI). • The most appropriate INITIAL test → Urine osmolality. *It is low in DI*. √ If you suspect diabetes insipidus (polyuria, polydipsia, hypernatremia), the initial test is → urine osmolality. (if < 800, then it is likely DI, we then proceed to plasma osmolality and fluid deprivation test). Imp √

	√ To differentiate central from nephrogenic DI, → Fluid deprivation test is done followed by desmopressin/vasopressin administration. Imp √ *What if you suspect DI but there is not (request urine osmolality) in the options? → pick fluid deprivation test and response to vasopressin.*
Key 158	Constipation, fatigue, body aches, high serum calcium, high parathyroid hormone, low serum phosphate, Hx of renal stones "colic" → Think 1ry hyperparathyroidism → Refer for parathyroidectomy. "Cinacalcet is reserved for patients who are unsuitable for surgery". **If no surgery in the options?** → Bisphosphonate (eg, alendronate) + Cinacalcet. (Bisphosphonates eg, alendronate is to improve bone density. And Cinacalcet is to correct hypercalcemia).

	Remember that hypercalcemia can cause fatigue, constipation, bone pain, stones.
Key 159	Nausea, vomiting, abdominal pain, low Na^+, high K^+ Others: Hyperpigmentation, weight loss, postural hypotension, fatigue Think → Addison's disease. Definite investigation → Short ACTH stimulation test (short Synacthen test).
Key 160	One fasting glucose test is <u>abnormal</u>. No polydipsia or polyurea. What is next? → Repeat fasting glucose level.
Key 161	MODY (Maturity Onset Diabetes in the Young). • *DM in a patient < 25 Y/O.* • *Strong FHx* (2 generations). It is *Autosomal Dominant*. • Mild Hyperglycemia.

	• Usually low BMI (thin patient). • No need for insulin initially. Responds to Sulphonylureas. → Refer to endocrinology for → Genetic counselling for maturity onset diabetes in the young (MODY). This is usually done before performing genetic tests. "*Remember that if the patient is symptomatic (e.g., polyurea, polydipsia, weight loss, polyphagia) and showing one DM test that's is abnormal → there is no need to repeat or request DM tests*".
Key 162	LADA (Latent Autoimmune Diabetes of Adulthood). • It is a variant of DM type 1 but is of insidious onset (develops much slower). So, usually diagnosed later in age 30-50 Y/O. usually thin as well. • Presence of any B cell antibody. • If suspected, request → GAD antibodies (glutamic acid decarboxylase Abs). • Rx → like type 2 DM (however, the need to insulin occurs earlier).
Key 163	Examples on Hyperthyroidism (Example 1) A patient with hyperthyroidism and a swelling of the right lobe of the thyroid gland.

Isotope scan shows → increased radioactive iodine uptake in a solitary region of the right lobe of the thyroid gland while it is low in the rest.

Both TPO (thyroid peroxidase) antibody and TSH receptor antibody are negative. What is the likely Dx?

√ TPO antibody and TSH receptor antibody are negative

→ NOT Graves.

√ increased radioactive iodine uptake in an isolated region of the right lobe

→ Solitary nodular goitre.

(Example 2) A pregnant woman in her 2nd trimester (25th week) presents to an endocrine clinic with a Hx of confirmed hyperthyroidism. She is not on any medications. She has smooth goitre. Her HR is 115.

TSH is low, Free T4 is high, Thyroid peroxidase (TPO) is positive

What is the most likely Dx and the most appropriate Rx?

◘ For Dx:

• TPO is positive → indicative of autoimmune disease (e.g., Graves in case of hyperthyroidism, or Hashimoto in case of hypothyroidism).

• Here, since T4 is high → hyperthyroidism → Grave's disease.

◘ For Rx:

• The safest Rx option for pregnant women is taking antithyroid medications (not surgery nor radioactive iodine).

• So, this patient should receive only carbimazole or propylthiouracil (PTU).

• PTU is preferable in women planning to get pregnant, or those in 1st trimester or postpartum.

• So, for this case (2nd trimester), carbimazole is preferred.

• However, if it is not among the options, pick (propylthiouracil).

• Propranolol is used for palpitations. Also, it does not treat the hyperthyroidism, and this pregnant woman needs her hyperthyroid to be controlled during pregnancy.

Key 164

Sheehan's Syndrome (Postpartum Hypopituitarism)

◙ Pituitary ischemia/ infarction due to severe postpartum hemorrhage.

Severe postpartum hemorrhage → severe hypotension

→ pituitary ischemia and necrosis → Hypopituitarism

→ ↓ in pituitary gland hormones (e.g., GH, TSH, Prolactin, LH, FSH, ACTH).

◙ The earlier and most important features to remember is

- Agalactorrhea (failure to lactate) "↓ prolactin → ↓ milk".
- Amenorrhea

◙ Others:

As TSH is low → lethargy, tiredness, weight gain, intolerance to cold.

◙ Dx:

- Best initial test → Provocative hormonal testing.

- Most accurate test → MRI of the pituitary gland and hypothalamus to rule out tumor or other pathology.

◙ Rx → Lifelong hormone replacement.

Example (1)

A 30 YO woman presents complaining of tiredness, feeling lethargic and a Hx of increasing weight over the past few months. She had vaginal delivery 6 months ago and at that time she suffered from a major postpartum

	bleeding. She had to feed her child a formula milk as she could not lactate him. Her menstrual cycles are absent since that event. • The likely Dx → Sheehan's syndrome. • The likely structure that results in her symptoms → Pituitary gland. Example (2) A 28-year-old woman, 7 days post vaginal delivery, presents to her child's pediatrician with a complaint that she is unable to breast feed her child. History reveals a vaginal delivery complicated by postpartum hemorrhage. • The likely Dx → Sheehan's syndrome = Postpartum hypopituitarism.
Key 165	◙ High or normal parathyroid hormone + high calcium + Low Phosphate → 1ry hyperparathyroidism. ◙ High parathyroid hormone + LOW calcium + High or N. Phosphate → 2ry hyperparathyroidism commonly due to vit. D deficiency. ◙ End-stage renal failure + high parathyroid hormone + high calcium + high Phosphate → Tertiary hyperparathyroidism.

	◙ Renal disease + LOW parathyroid hormone + high calcium + high Phosphate + Hx of smoking → Bone metastasis possibly due to lung cancer.
Key 166	Low sodium (hyponatremia) + Low serum osmolality + High urine Osmolality Think → SIADH (syndrome of inappropriate antidiuretic hormone secretion). --- In SIADH: Hyponatremia (low Serum Sodium), Low Serum Osmolality, High Urine Osmolality. In Diabetes Insipidus: Hypernatremia (high serum sodium), Low Urine Osmolality, High Serum Osmolality. *(The urine osmolality increases after giving vasopressin)* *What is low?* *In SIADH → Sodium and Serum osmolality are ↓.* *In DI → urine osmolality is ↓.* ---

	In water overload and glucocorticoid insufficiency: Low serum sodium (hyponatremia). However, urine osmolality will be normal or decreased.
Key 167	In diabetic patients who have heart failure "HF" with reduced ejection volume or in those who are at risk of cardiovascular disease in addition to metformin, Give → SGLT2 inhibitors such as Dapagliflozin, Empagliflozin, Canagliflozin. (When SGLT2 inhibitors are added to the medications of HF which are B-blockers, ACE inhibitors, Aldosterone antagonist → reduce cardiovascular death). • SGLT-2 inhibitors (Gliflozin) have an important side effect to remember → Genital infections eg, balanoposthitis (erythema and itchiness on the penis glans and prepuce).
Key 168	Patients with low serum vitamin D levels requires → Supplements of calcium and vitamin D Even if they need bisphosphonate (eg, alendronic acid) as in case of osteoporosis or DEXA ≤ -2.5, if they are deficient in vitamin D, they still need vitamin D and calcium supplements before initiating bisphosphonate.

Key 169

Hyperparathyroidism VS Other Important DDx

(All Given Scenarios Have been Asked Previously in the Exam)

	Primary hyperparathyroidism	Secondary hyperparathyroidism	Tertiary hyperparathyroidism
PTH	↑/N	↑	↑↑↑
Ca2+	↑ *	↓/N	↑
P04+	↓	↑/N	↑
Vitamin D	N/↓	↓↓↓	↓/N
Comments	In 85% a solitary parathyroid adenoma is present Important differential diagnosis is FHH Familial Hypocalciuric Hypercalcemia	Causes include: • chronic renal failure • vitamin D deficiency Prolonged Hypocalcemia stimulates the excessive release of PTH	Caused by: • end stage renal failure

Scenario (1):

A 45 YO female presents with increased thirst and increased urination. Her calcium is 2.9 (normal is 2.1-2.6). Her phosphate is 0.7 (normal is 0.8-1.4). Her parathyroid hormone is 8.4 (normal is 0.8-8.5).

The likely Dx → Primary Hyperparathyroidism.

PTH → Normal
Calcium → High (Featured also by the polydipsia and polyuria).
Phosphate → Low

Scenario (2):

A 60 YO woman presents with the followings:

√ Confusion. √ Weakness. √ Pains and aches. √ Polyuria and Polydipsia.

√ Hx of renal calculi. √ High parathyroid hormone level. √ High serum calcium.

√ Low serum phosphate. √ Normal eGFR.

Interpretation and most likely diagnosis:

↑ or normal PTH, ↑ Ca++, ↓ Ph → think 1ry hyperparathyroidism.

◙ Refer for parathyroidectomy. "*important*"

"Cinacalcet is reserved for patients who are unsuitable for surgery".

√ This woman likely has primary hyperparathyroidism.

√ The commonest cause of 1ry hyperparathyroidism is → Parathyroid Adenoma.

√ The features presented are due to Hypercalcemia (bone aches, confusion, renal calculi, excessive thirsty and urination).

√ Note that in 2ry hyperparathyroidism, the Ca++ would be low, and also the eGFR would not be normal.

Scenario (3):

A 60 YO man presents with: End-stage renal failure + high parathyroid hormone + high calcium + high Phosphate

→ Tertiary hyperparathyroidism.

Scenario (4): Caution!

A 72 YO man presents complaining of generalized lethargy and weakness, increased urinary frequency and increased thirst. He smokes 20 cigarettes a day. He is a smoker for the past 40 years of life. Lab investigations show: High calcium – high phosphate – slightly low parathyroid hormone – normal vit. D
His renal function tests are deranged: high urea and creatinine, low eGFR.
Which of the following is the most likely Dx?
[1ry hyperparathyroidism ▌Tertiary hyperparathyroidism ▌Lung malignancy].

- In 1ry hyperparathyroidism → ↑PTH, ↑Ca, ↓Ph
- Here, PTH is ↓ → so, not 1ry Hyperparathyroidism.

√ In Tertiary hyperparathyroidism → ↑PTH, ↑Ca, ↑Ph, End-stage renal disease.

√ Although in this patient there is ↑Ca, ↑Ph and Renal Disease, take care that parathyroid hormone here is LOW → So, not tertiary hyperparathyroidism.

◙ Given the long Hx of smoking → Lung malignancy is a high possibility → Lung cancer easily metastasizes to BONEs → Leading to Hypercalcemia (seen here).

◙ Hypercalcemia can cause ↑urinary frequency and ↑ thirst.

Scenario (5): Caution!

A 66 YO woman presents complaining of back pain that has been worsening over the past 5 months. Her labs are as follows:

Slightly low calcium – Normal phosphate – High parathyroid hormone – Low vit. D
Her renal function tests are Normal.
Which of the following is the most likely cause of her symptoms and labs?
[1ry hyperparathyroidism ▌Pseudohypoparathyroidism ▌Vit. D deficiency].

• In 1ry hyperparathyroidism → ↑PTH, ↑Ca, ↓Ph

• Here, Ca is ↓, and Ph is Normal → so, not 1ry Hyperparathyroidism.

√ Pseudohypoparathyroidism → ↑PTH, ↓Ca, ↑Ph.

(it is congenital, hypocalcemia associated with high PTH and high Phosphate).

◙ The case here is likely 2ry hyperparathyroidism caused by vit. D deficiency.

In 2ry hyperparathyroidism → ↑ PTH, ↓Ca, (↑ or Normal Ph).

	Vitamin D deficiency → leads to decreased absorption of calcium in the GIT → Leads to Hypocalcemia → Which stimulates ↑ PTH release. (2ry Hyperparathyroidism). --- Scenario (6): A 58-year-old man presents to the GP surgery for lethargy and being thirsty most of the time. He takes multivitamins. His blood results show: Normal sodium, potassium, creatinine, eGFR, TSH, ALT, AST, ALP. Serum corrected calcium is 2.9 mmol/L (2.1-2.6). Parathyroid hormone (PTH) is 8.4 mmol/L (0.8-8.5). What is the most likely diagnosis? → Primary hyperparathyroidism. In 1ry Hyperparathyroidism, calcium is high, PTH is high or normal. PTH here is at the upper limit of normal value. If this is a case of vitamin D overdose, calcium will be ↑ but PTH would be ↓.
Key 170	Remember that Sepsis or surgery can lead to an acute exacerbation of chronic insufficiency (Addison disease, Hypopituitarism). → Addisonian Crisis (Severe nausea, vomiting, abdominal pain, Severe weakness and confusion, Hypotension, Hyponatremia, Hypoglycemia, Hyperkalemia). Shortage (↓) of 3S → Salt (low Na^+ but high K^+), ↓ Sugar, ↓Steroid, ↓BP.

	♣ Management of Addisonian crises: ♦ First step → IV Hydrocortisone 100 mg (intravenously). Important √ It can be given IM if no IV access is possible. Hydrocortisone would correct hypotension, hyponatremia and hyperkalemia. ♦ Then → 1 litre normal saline infused over 30-60 mins or with dextrose if hypoglycaemic. ♦ Continue hydrocortisone 6 hourly until the patient is stable. No fludrocortisone is required because high cortisol exerts weak mineralocorticoid action. ♦ Correct hypoglycemia if present. It is important to remember that the first immediate step is → IV hydrocortisone. FOLLOWED by IV normal saline.
Key 171	**Remember:** • Normal Ca + Normal Phosphate + Normal ALP ➔ **Osteoporosis**. • Normal Ca + Normal Phosphate + High ALP ➔ **Paget's disease**. • Low Ca + Low Phosphate + High ALP ➔ **Osteomalacia**. **Osteomalacia**: • Alkaline phosphatase is high, Ca^{++} and Phosphate are low.

	• Sometimes, the stem may only give you that Alkaline phosphate is high without mentioning that the patient has low calcium or phosphate. • In this case, other hints towards low Vit D will be given. • For examples, muscle aches, proximal muscle weakness, the patient does not go out frequently (lack of exposure to sunlight), poor diet (not enough Vit D intake). N.B. Proximal muscle weakness and pain are features of Vit D deficiency; thus osteomalacia.
Key 172	The link between Gliflozin and DKA. • It is important to remember that patients with type 2 DM who are taking SGLT-2 inhibitors (gliflozin) eg, Canagliflozin have an increased risk of developing diabetic ketoacidosis (DKA). • It is interesting that sometimes SGLT-2 inhibitors (gliflozin) can cause euglycemic DKA (ie, the patient presents with all features of DKA such as nausea, vomiting, abdominal pain, diarrhea, dehydration, extreme lethargy but the random blood glucose is not elevated (ie, < 11.1 mmol/L). • In such a case, we need further quick tests to confirm DKA (important), eg: → Capillary ketones (quick and accurate), Urinary ketones, Blood gas. • The first step would be rehydration (IV fluids).
Key 173	In diabetic patients who have heart failure "HF" with reduced ejection volume Give → SGLT2 inhibitors such as Dapagliflozin, Empagliflozin

	(When SGLT2 inhibitors are added to the medications of HF which are B-blockers, ACE inhibitors, Aldosterone antagonist → they reduce cardiovascular death). So, in DM with heart failure (or risk for cardiovascular disease eg, family history), use metformin and flozin family eg, Dapagliflozin, Empagliflozin, Canagliflozin. Note that SGLT2 inhibitors (Flozin family) can also help in weight loss.
Key 174	Weight gain + easy bruising + ↑ BP + abdominal striae + weakness + ↓K^+ • Think → Cushing syndrome. • Initial tests → 24-hour urinary cortisol, overnight dexamethasone suppression.
Key 175	**A head injury followed by increased urination (polyuria) and increased water drinking (polydipsia). Serum sodium is high (hypernatremia).** √ Think → Diabetes insipidus (cranial = central). √ The most likely abnormal value → Plasma and urine osmolality. In DI → hypernatremia, ↑serum -plasma- osmolality, ↓urine osmolality. (Electrolyte abnormalities eg, hypokalemia and hypercalcemia can be seen in **nephrogenic** diabetes insipidus not in **central** diabetes insipidus). • Cranial diabetes insipidus can be idiopathic or due to head injury or pituitary gland surgery. The mechanism is that there becomes a decreased

	in the secretion of the antidiuretic hormone (ADH) from the pituitary gland). • In nephrogenic diabetes insipidus, there is normal secretion of ADH but there is insensitivity to ADH. • Note that in diabetes insipidus, there is hypernatremia (↑ serum Na+), whereas is SIADH and Addison's disease, there is hyponatremia.
Key 176	Headaches + Hypertension + Sweating + ↑ Insulin-like growth factor (IGF-1) Think → Acromegaly.
Key 177	↑ serum alkaline phosphate + ↓ serum calcium (even if slightly low) + Proximal muscle weakness (eg, hips, shoulders) Think → Osteomalacia. In **osteomalacia**: the patient should be prescribed both: vitamin D and calcium supplements. However: If you have to pick one of the two, pick vitamin D supplements. (Important √).

	Remember: • Normal Ca + Normal Phosphate + Normal ALP ➔ **Osteoporosis**. • Normal Ca + Normal Phosphate + High ALP ➔ **Paget's disease**. • Low Ca + Low Phosphate + High ALP ➔ **Osteomalacia**.
Key 178	Important Note to Remember: Any diabetic patient (either DM 1 or 2) who has hypertension and his ACR (urine Albumin: Creatinine ration) is ≥ 30 mg/mmol should be started on → ACE inhibitors (eg, lisinopril) unless contraindicated. • Increased urine ACR means increased albuminuria. • ACE inhibitor could control the hypertension and protect kidneys.
Key 179	**NOTE**: Thyroid Goitres that cause local neck compression symptoms (eg, voice changes, difficulty swallowing, may cause chocking while lying flat is preferred to be treated with surgery (eg, **subtotal thyroidectomy**).
Key 180	• Remember to suspect adrenal insufficiency in patients who have stopped corticosteroids (eg, prednisolone) after a prolonged use.

	• Stoppage of prednisolone after a prolonged usage may lead to adrenal atrophy. This may lead to specific and or non-specific symptoms. ◙ To confirm adrenal insufficiency: → Short ACTH stimulation test (short Synacthen test). Important √.
Key 181	**Hypercalcemia**: • The first step in the management of elevated serum calcium (eg, in bone metastasis, in 1ry hyperparathyroidism, TB, Sarcoidosis) → IV fluids (= IV sodium chloride). √ • The 2nd line → Bisphosphonate (eg, Alendronate, Risedronate, Pamidronate). ◙ Remember that hypercalcemia manifestations include: Confusion, polyurea, polydipsia, low moods, bone pain, constipation, stones. --- **Hypocalcemia**: • The first step in the management of low serum calcium → Calcium gluconate. √

	If both low serum calcium and low vitamin D are present → The (initial) step in acute hypocalcemia (presenting with tetany, seizures, or serum calcium level less than 1.9 mmol/L) is slow IV injection of 10 ml of calcium gluconate 10%. The patient would also receive vitamin D supplements. However, calcium gluconate is the initial step. ◙ Remember that hypocalcemia manifestations include: SPASMODIC **Neuronal Hyperexcitability** Spasms, Perioral Paraesthesia, Anxious, Seizures, Muscle tones increased in smooth muscles, Orientation impaired and confusion, Dermatitis, Impetigo Herpetiform (rare and serious), Chvostek's sign, Cardiomyopathy (prolonged QT interval on ECG). - Trousseau's signs → after occlusion of brachial artery → *wrist flexion* - Chvostek's sign → Tapping over parotid → *twitching of facial muscles*.
Key 182	◙ What is the treatment of choice for **hyperthyroidism**? In general, → Carbimazole unless in the following conditions: Note (1): if the patient is a woman in her 1st trimester pregnancy, or is planning to get pregnant soon, use → propylthiouracil (PTU) instead. Note (2): if the patient presents with thyroid storm -thyroid crisis- (eg, altered mental status, high fever, vomiting, multisystem decompensation - cardiac failure, respiratory distress etc- → propylthiouracil (PTU) instead.

Also, in thyroid storm, we give a beta-blocker (propranolol) to control palpitations and tremors.

Carbimazole is given once a day while PTU is given twice or thrice a day.

Also, there is a small risk of liver injury with PTU.

◙ When to use thyroidectomy to treat hyperthyroidism?

√ Poor compliance with antithyroid medications.

√ Severe Grave's ophthalmopathy.

√ Relapsing Grave's disease.

√ Local compression of the enlarged thyroid causing difficult breathing.

Example:

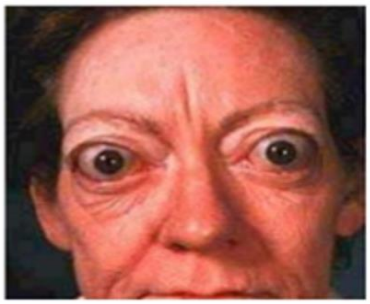
A 42-year-old woman presents to the GP complaining of palpitations over the last few weeks. She has recently lost 4 kg of her weight over the last 5 weeks despite having a good appetite. She feels she is more sweaty than usual. TSH is found to be low, T3 and T 4 are high. She has a right lobe neck swelling on palpation. She was given propranolol. What is the most appropriate management?

→ Carbimazole.

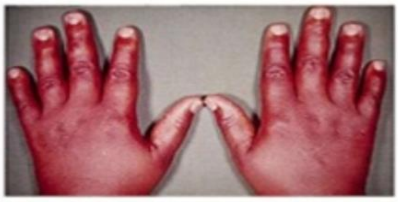
• She has hyperthyroidism (low TSH, high T3 and T4) + weight loss despite eating, feeling hot and more sweaty than usual, palpitations and tachycardia, fine tremors.

	• She is not planning to get pregnant soon, not in 1st trimester pregnancy and not having thyroid storm → So, PTU is not preferred. • She does not have any indications of thyroidectomy (eg, local compression causing difficult breathing, severe Grave's ophthalmopathy, relapsing Grave's).
Key 183	**Grave's Disease**. • Autoimmune disease that leads to hyperthyroidism. • **Manifestations of Grave's:** Manifestations of hyperthyroidism (eg, weight loss despite good appetite, tremors, tachycardia and palpitations, feeling hot and sweaty), **+** Ophthalmopathy (eg, periorbital edema, lid lag, lid retraction). ◙ **Lab** → ↓TSH ▌↑T3,4 ▌**+ve** autoantibodies (TPO). ◙ **First line Rx** → Antithyroid drugs (eg, carbimazole, PTU). If relapsing Grave's or if with severe ophthalmopathy or if large mass causing difficult breathing → Thyroidectomy.

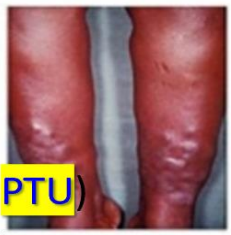
Graves disease



1. Eye signs – exomphalos, ophthalmoplegia, lid lag and lid retraction
2. Pretibial myxoedema
3. Thyroid acropathy



+ Manifestations of **hyperthyroidism** (eg, weight loss despite good appetite, tremors, tachycardia and palpitations, feeling more hot)



◙ **Lab** → ↓TSH ▌↑T3,4 ▌+ve autoantibodies (TPO)

◙ **First line Rx** → Antithyroid drugs (eg, carbimazole, PTU)
If relapsing Grave's or if with severe ophthalmopathy or if large mass causing difficult breathing → Thyroidectomy.

Key 184

♠ In a patient with **hypothyroidism** who is on **levothyroxine**, if the TSH is still high and T3 and/or T4 is still low

→ Increase the dose of the Levothyroxine.

Note:

If a patient is with a background of hypothyroidism and is already taking levothyroxine but still symptomatic (eg, feeling lethargic, gaining weight, feeling cold etc.) → check his TSH.

If the **TSH** is still **high** → Increase the dose of levothyroxine (even if T4 is within normal range). This case is called (undertreated hypothyroidism).

(We depend on TSH in determining the dose of levothyroxine, not T4 or 3).

Key 185

Reminder:

Diabetes insipidus (Polyurea, Polydipsia).

- Central (Cranial) DI → (↓ ADH secretion) → eg, after head trauma.
- Nephrogenic DI → Increase ADH resistance in the kidneys.

Quick important comparison:

Syndrome of inappropriate ADH	Diabetes insipidus
Hyponatremia (↑serum Na^+)	Hypernatremia (↑serum Na^+)
Low serum osmolality	High serum osmolality
High urine osmolality	Low urine osmolality (*The urine osmolality increases after giving vasopressin*)

What is the low?

In SIADH → Sodium and Serum osmolality.

In DI → urine osmolality.

	Q) A head injury followed by increased urination (polyuria) and increased water drinking (polydipsia). Serum sodium is high (hypernatremia). √ Think → Diabetes insipidus (cranial = central). √ The most likely abnormal value → Plasma and urine osmolality. In DI → hypernatremia, ↑serum -plasma- osmolality, ↓urine osmolality. (Electrolyte abnormalities eg, hypokalemia and hypercalcemia can be seen in **nephrogenic** diabetes insipidus not in **central** diabetes insipidus).
Key 186	**Headaches + Palpitations + Hypertension + Anxiety and Sweating** • **Think** → Pheochromocytoma. ◙ **Remember: Mnemonic→ PHEochromocytoma** **P** → Palpitations. **H** → Headache, Hypertension **Ph** → Flushing (sweating). **E** → Episodic (Paroxysmal). • **What hormones are raised?** → Catecholamines (adrenaline and noradrenaline). • **Diagnosis?** → 24 hours collection of urine metanephrines (not catecholamines).

Key 187	**Don't Make the Following Normal Values Fool You:** • **Parathyroid hormone** is typically **elevated** in the following conditions; however, it can be normal: Primary hyperparathyroidism, vitamin D deficiency, osteomalacia. • In Conn's syndrome, serum **potassium** is usually **decreased** (70%), however, it can be normal. (Sodium can also be normal). • **Blood pressure** in pheochromocytoma is typically **elevated**. However, in around 10%, it is normal (normotensive).
Key 188	**For Neuropathic pain:** **(Eg, a diabetic patient has tingling, numbness burning pain in his feet)** → **Gabapentin**, **Amitriptyline**, **Pregabalin**, **Duloxetine** Anyone could be the correct answer (imp √). **Memorise them all by this Mnemonic:** **A**way, **G**oes, **D**a, neuropathic **P**ain: **A**mitriptyline, **G**abapentin, **D**uloxetine, **P**regabalin.

Key 189	**A Scenario on Diabetes:** A 52-year-old man has just undergone a cholecystectomy. After the operation, one of the results of his blood tests is a high serum glucose level (12 mmol/L). His HbA1c is 68 mmol/mol (the normal is <48). His blood pressure is 140/80. His BMI is 27 kg/m2. What is the most appropriate management? A) Reassure. B) Start metformin. C) Start empagliflozin. D) Start amlodipine. E) Start enalapril. **Answer → B.** • One might think this is a case of **stress hyperglycemia** because of the surgery that would resolve in a few hours and pick (reassure). This is **wrong**. If it is a stress hyperglycemia, HbA1c would not have been elevated. Remember, HbA1c measures the average blood glucose levels over the past 3 months. • Regarding the **high blood pressure**, it is not so high. Plus, it should be repeated and ABPM may be required to decide whether he is a

	hypertensive patient or not. So, antihypertensive agents (amlodipine, enalapril) are **wrong**. • So, he is a diabetic patient, and overweight, the first-line → Metformin. Quick note on Biguanides (metformin): although it reduces weight and it is considered the first line hypoglycemic drug for DM type 2, it is contraindicated in renal impairment (GFR< 30) and the dose should be reduced if GFR<45.
Key 190	A diabetic patient on metformin and gliclazide which control his blood sugar adequately (HbA1C is normal). However, he has frequent falls (with blurry vision and dizziness right before the fall). What to do? → These falls are likely due to hypoglycemia caused by gliclazide. → Gliclazide (sulphonylureas) has risk of hypoglycemia. → Stop gliclazide.
Key 191	**Postpartum Thyroiditis:** An inflammatory condition of the thyroid gland, can occur after childbirth. **It includes 2 phases:** • **Hyperthyroid phase**: starts 4-6 months postpartum. (It is transient; thus, the treatment is supportive by giving betablockers eg, **propranolol**: for palpitation, tremor, anxiety)/

	• **Hypothyroid phase** (levothyroxine can be considered if symptomatic).
Key 192	**What is the first-line therapy for postmenopausal osteoporosis to reduce the risk of fractures?** → Bisphosphonates (eg, alendronic acid).
Key 193	**◙ Important Antibodies in Autoimmune Thyroid disease:** • **Hashimoto thyroiditis** (Autoimmune **hypothyroidism**): → Anti-TPO antibodies. They can also be present in Graves's disease but not specific to it. • **Grave's disease** (Autoimmune **hyperthyroidism**): → Anti-TSHR antibodies. (Most specific to Grave's). √ Remember: in Grave's disease, there are **eye manifestations** eg, *lid lag*, *lid retraction*, *exophthalmos*, *gritty sensation in eyes*, *proptosis*.
Key 194	**Parathyroidectomy** is the most definitive treatment for patients with primary hyperparathyroidism especially symptomatic patients and in those who have osteoporosis or fractures. **√** ***Bisphosphonates*** are used to treat osteoporosis but **not** 1ry hyperparathyroidism. While they may help improve bone density, they do not address the underlying cause of 1ry hyperparathyroidism.

	The most common cause of primary hyperparathyroidism is → Parathyroid adenoma, mainly **solitary parathyroid adenoma**.
Key 195	A type 1 diabetes mellitus (T1DM) patient is on the following regimen: • 20-24 units of Long-acting insulin (taken at night). • Variable doses of short acting insulin (taken with meals). His glucose levels are within target range throughout the day (postprandial, in the evening, and overnight) except in the morning it is elevated. He is following dietary and exercise guidelines. His HbA1C is 66 mmol/mol which is above the target (<53). What should be done? Since the only elevated glucose level is in the morning, → Increase the dose of long-acting insulin that is taken at night.
Key 196	The initial fluid therapy in a patient with diabetic ketoacidosis if SBP < 90 is: → 500 ml of 0.9% sodium chloride over 15 minutes. "Normal saline **bolus**". **Followed by a continuous rate "infusion":**

	√ If Systolic BP is > 90, the bolus can be given over 1 hour.
Key 197	**◙ The ultrasound findings in hyperparathyroidism:** • Primary hyperparathyroidism → Parathyroid adenoma (mainly solitary). • Tertiary hyperparathyroidism → Hyperplasia of parathyroid glands.
Key 198	**Quick Summary of Klinefelter Syndrome** **Definition**: • Klinefelter Syndrome is a genetic condition in males characterized by an extra X chromosome (47, XXY instead of the usual 46, XY). **Symptoms**: • **Physical**: ◦ Tall stature with long legs and shorter torso. ◦ Reduced muscle mass and strength. ◦ Small testes and reduced testosterone production. ◦ Gynecomastia (enlarged breast tissue). ◦ Sparse facial and body hair. ◦ Delayed or incomplete puberty. ◦ Infertility due to low sperm production. • **Cognitive and Behavioural**: ◦ Learning disabilities, especially in language and reading. ◦ Delayed speech and language development. ◦ Attention and memory problems.

- Social and emotional difficulties, such as shyness and low self-esteem.

Diagnosis:

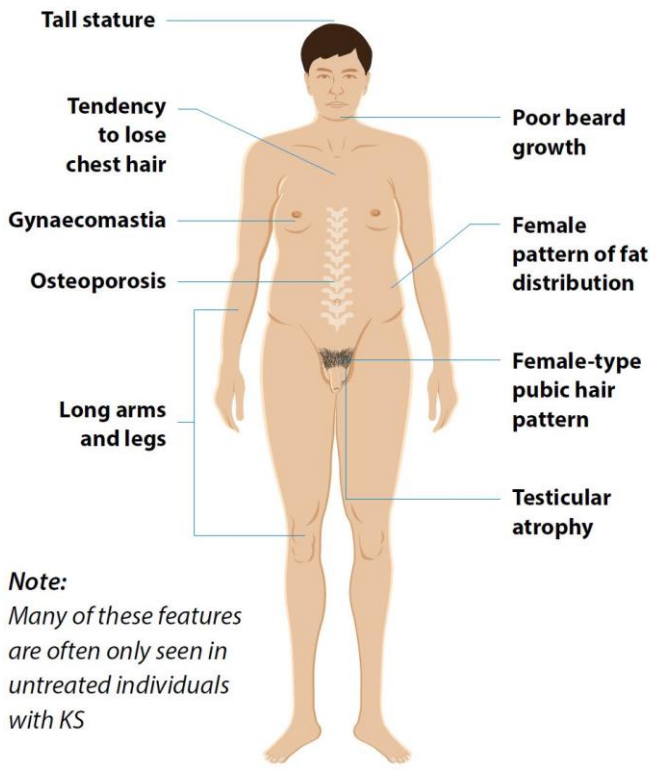
- **Karyotype Analysis (for definitive diagnosis)**: Identifies the presence of an extra X chromosome.
- **Hormone Testing**: Shows abnormal levels of hormones such as testosterone.
- **Physical Examination**: Reveals characteristic physical features and developmental issues.

Treatment:

- **Testosterone Replacement Therapy (First Line)**: Helps develop secondary sexual characteristics and improve muscle mass, mood, and energy levels.
- **Fertility Treatment**: Assisted reproductive technologies may help some men with Klinefelter syndrome father children.
- **Educational Support**: Tailored educational interventions to address learning disabilities.
- **Speech and Physical Therapy**: Helps improve communication skills and physical strength.
- **Psychological Support**: Counselling and support groups for emotional and social challenges.

Asked Previously: What is the initial treatment for Klinefelter syndrome?

→ Testosterone replacement therapy.



Key 199

Important Notes on Diagnosing Grave's Disease:

• The initial test for Grave's Disease is → Thyroid function test.

• The most specific diagnostic test for Grave's disease is

→ Anti-thyrotropin receptor (Anti-TSH receptor) antibodies. On the other hand, anti-TPO antibodies are associated with various autoimmune diseases, not only Grave's.

Key 200

A Scenario on Diabetes Mellitus Type 1

A 25-year-old woman with type 1 diabetes mellitus attends a follow-up consultation. She has been monitoring her blood glucose at home and presents a diary of her recent readings to the healthcare provider. Her current insulin regimen involves rapid-acting insulin before each meal and long-acting insulin administered at night. The following are her recorded glucose levels over the past week:

Day	Fasting (Before breakfast) (mmol/L)	Pre-lunch (mmol/L)	Pre-dinner (mmol/L)	Bedtime (mmol/L)
Monday	10.2	5.3	5.9	5.0
Tuesday	11.8	5.6	5.5	4.7
Wednesday	10.5	5.4	6.0	5.1
Thursday	9.6	5.5	5.8	4.6
Friday	10.9	5.2	6.1	5.3
Saturday	12.0	5.7	5.9	5.2
Sunday	9.8	5.4	6.2	5.0

What is the most appropriate adjustment to her insulin regimen?

A) Increase the dose of rapid-acting insulin before dinner.

B) Decrease the morning dose of rapid-acting insulin.

C) Increase the nighttime dose of long-acting insulin.

D) Decrease the nighttime dose of long-acting insulin.

E) Increase the dose of rapid-acting insulin before breakfast.

The correct answer is **C) Increase the nighttime dose of long-acting insulin**.

Explanation:

- Fasting blood glucose levels are considered high (indicating hyperglycaemia) when they exceed **7.0 mmol/L**. According to most clinical guidelines, fasting blood glucose levels in people without diabetes should typically be between **4.0 and 5.9 mmol/L**, and for those with diabetes, the target is usually between **4.0 and 7.0 mmol/L**.

- The patient's fasting blood glucose levels are consistently high, ranging from 9.6 mmol/L to 12.0 mmol/L. This suggests that the **basal insulin**, which is **long-acting** and typically given at **bedtime**, is insufficient.

	• Long-acting insulin, which is taken at bedtime, is responsible for controlling blood glucose during the fasting period (overnight). Since her glucose levels are high upon waking, it indicates that the current dose of long-acting insulin is insufficient. • The pre-lunch, pre-dinner, and bedtime glucose levels are all within the target range, meaning that her rapid-acting insulin before meals is effectively controlling postprandial (after meals) glucose. Thus, there is no need to adjust the rapid-acting insulin doses at this time. Therefore, **increasing the nighttime dose of long-acting insulin** is the most appropriate adjustment to help lower her fasting glucose levels and improve overall glucose control.
Key 201	**A Scenario on Hyperthyroidism Management in Pregnancy** A 30-year-old woman attends her 28-week antenatal check-up. She has a history of hyperthyroidism secondary to Graves' disease and has been on propylthiouracil (PTU) since her pregnancy began. Recent thyroid function tests show stable control of her thyroid levels, with slightly low TSH but normal free T4 levels. She has no symptoms of hyperthyroidism and feels

generally well. What is the most appropriate next step in managing her hyperthyroidism during pregnancy?

A) Refer for thyroidectomy.

B) Stop all antithyroid medications.

C) Continue propylthiouracil only.

D) Initiate levothyroxine only.

E) Switch from propylthiouracil to carbimazole and add levothyroxine.

The correct answer is **C) Continue propylthiouracil only.**

Explanation:

- **Continuing PTU** is preferred during the first trimester to avoid potential teratogenic effects of carbimazole. By the second trimester, many clinicians switch to carbimazole due to the risk of hepatotoxicity with prolonged PTU use. However, if thyroid function is well-controlled and liver function is stable, PTU can be continued.
- **Carbimazole** is typically used after the first trimester, but switching from PTU to carbimazole is not mandatory if the patient's condition is stable,

and no liver toxicity is evident. Moreover, switching to Carbimazole in the 2nd trimester may be considered, however; the option (E) includes adding a levothyroxine "which is used for hypothyroidism", making the option invalid.

- **Stopping antithyroid medications** can lead to a rebound of hyperthyroidism, which may have serious consequences for both the mother and fetus, including preterm labour or pregnancy complications.
- **Levothyroxine alone** is not appropriate here, as the patient needs treatment for hyperthyroidism, not hypothyroidism.
- **Thyroidectomy** is reserved for cases where antithyroid medications are not effective or not tolerated, which is not the case here.

Summary: In this case, the patient's thyroid function is well-controlled with PTU, and there are no signs of hepatotoxicity. Therefore, continuing PTU is the best management approach to maintain stability during the pregnancy while minimising risks to the fetus.

Management of Thyrotoxicosis (Hyperthyroidism) in Pregnancy

- **Preconception and First Trimester:**

- **Propylthiouracil (PTU)** is preferred before pregnancy "if a woman is planning to get pregnant" and during the first trimester due to its lower risk of causing congenital malformations compared to carbimazole.

- **Second and Third Trimester:**
  - **Carbimazole** is preferred in the second and third trimesters to reduce the risk of PTU-related hepatotoxicity. Carbimazole is also the standard choice for long-term management in non-pregnant individuals.
- **Risks of Carbimazole:**
  - Carbimazole can cause fetal complications such as **aplasia cutis** (a condition where skin, particularly on the scalp, is absent at birth) and **omphalocele** (a birth defect in which organs, such as the intestines or liver, develop outside the abdomen). This is why it is avoided in the first trimester.
- **Risks of PTU:**
  - **PTU** carries a significant risk of **hepatotoxicity**, especially with prolonged use, and is typically switched to carbimazole after the first trimester.
- **Crossing the Placenta:**
  - Both PTU and carbimazole cross the placenta, so the **lowest effective dose** should be used to minimise fetal exposure.
- **Radioiodine Therapy:**

- **Radioiodine** is contraindicated during pregnancy due to its ability to destroy the fetal thyroid gland, leading to fetal harm.

- **Partial Thyroidectomy:**
  - **Partial thyroidectomy** can be performed in the **second trimester** if hyperthyroidism cannot be controlled with medication. The second trimester is the safest time for surgery during pregnancy.
- **Preferred Treatment in Pregnancy:**
  - **Antithyroid medications** (PTU in the first trimester, carbimazole in the second and third trimesters) are the safest and most effective treatment for hyperthyroidism in pregnancy.

Q1) If there was a choice for: Stop PTU and Change to Carbimazole. Would it be correct?

Yes, **switching from PTU to carbimazole** can be considered a correct option, but it depends on the clinical situation. Here's why:

- **First Trimester**: Propylthiouracil (PTU) is preferred during the first trimester of pregnancy to reduce the risk of teratogenic effects associated with carbimazole and methimazole.
- **Second and Third Trimester**: After the first trimester, many clinicians switch from PTU to carbimazole due to the risk of **hepatotoxicity** with

prolonged PTU use. Carbimazole is generally considered safer for continued use in the second and third trimesters if liver function is a concern.

So, if there was an option to **stop PTU and switch to carbimazole** in the second trimester or beyond, it would be a valid option, especially if there were concerns about liver toxicity or long-term use of PTU.

Q2) So, why is the option [E) Switch from propylthiouracil to carbimazole and add levothyroxine] incorrect?

The option **(E) Switch from propylthiouracil to carbimazole and add levothyroxine** is incorrect because:

1. **Levothyroxine should not be added** when switching from PTU to carbimazole in the management of hyperthyroidism.
    - **Levothyroxine** is a replacement therapy for **hypothyroidism**, not hyperthyroidism. In this scenario, the patient has **hyperthyroidism**, and adding levothyroxine would unnecessarily increase thyroid hormone levels, worsening the hyperthyroidism.
2. The "block and replace" regimen (where antithyroid drugs are combined with levothyroxine) is generally **not recommended in pregnancy** because it involves completely blocking thyroid hormone production with high doses of antithyroid drugs and then replacing it with levothyroxine. This

	can pose risks to the fetus, such as inducing hypothyroidism, which can impair fetal development. Therefore, this regimen is avoided in pregnant women.